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Ann Arbor, Michigan

Sixteenth Annual Clinical Session, San Francisco, California, April 4-8, 1932

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Observations on Rheumatic Pancarditis and Infective Endocarditis*

By W. S. Thayer, M.D., F.A.C.P., *Baltimore, Md.*

We now know that the endocarditis of rheumatism on which so much stress has been laid in the past is but one of the manifestations of a general process, the most important feature of which, though often not the most prominent, is the cardiac disease. This cardiac disease is a general involvement of the heart in which valvular affections, acute, subacute and chronic, often, but by no means always, play a relatively important part. Indeed in the more acute and not infrequently in the more chronic forms of the malady the changes in the muscle or in the pericardium are of graver import than the sometimes more obvious endocarditis. There are other manifestations of rheumatic fever beside those in the joints and in the heart, notably changes in vessels, skin and nervous system which are rather characteristic.

That the rheumatic process is infectious is reasonably clear. That this infection is related to certain forms of streptococci is not improbable but cannot be said to have been proven. The nesting of bacteria at the seats of the characteristic focal lesions has not been demonstrated, and the inviting hypotheses of Weintraud, Benzançon, Swift, Coburn and others who believe that the lesions and symptoms of the rheumatic disease may be dependent upon an allergic process like that observed in syphilis or tuberculosis are not universally accepted.

Doubtless of infectious origin rheumatic heart disease may yet be distinguished from that which we call "bacterial" or "infective" endocarditis. Here the endocarditis, focal lesions on valves, mural endocardium or the intima of a larger vessel, is the essential seat of the disease, the spot at which is kept alive the infection to which, more or less directly, death is usually due.

The following observations are based largely on a study of sixty-five cases of rheumatic endocarditis with necropsy, fatal during a period of activity of the rheumatic process, along with a series of three hundred and six cases of infective endocarditis of which two hundred and six came to necropsy†.

*Presented at the Baltimore meeting of the American College of Physicians, March 23, 1931.

†The Gibson Lectures, Edinb. Med. Jr., 1931, n. s., xxxviii, 237-265, 307-334. In this article numerous references to the literature may be found which have not been included in this communication. For further references the reader is referred to the admirable monograph of Lemierre and Deschamps: Les endocarditis infectieuses, diagnostic et traitement, 1930, 8°, G. Doin et Cie., 1930.

It is possible to distinguish roughly two forms of rheumatic heart disease: (1) The acute malignant pancarditis occurring usually in youth with high fever, pronounced leucocytosis and general appearances which might easily be associated with an acute bacterial endocarditis. In such cases death may result within a few weeks, or, gradually, the process may become subacute and end in recovery with surprising improvement in the apparent cardiac impairment but with a resultant chronic valvular disease. Sometimes the fever pursues so regular an intermittent course and lasts so long that the picture may resemble a subacute or chronic vegetative endocarditis. (2) The more subacute and chronic forms of the disease. Here, while the onset is usually characteristic of an acute rheumatic fever, yet sometimes the arthritis, the fever, the signs of cardiac involvement may for long periods be so slight and indefinite that disease of the heart may be unsuspected. This is especially true in early childhood.

There are certain rather distinctive features of rheumatic heart disease.

Rheumatic carditis is essentially a disease of youth and adolescence. Nearly three-quarters of our fatal instances of rheumatic endocarditis with necropsy died in the first and second decades. How striking this phenomenon is is emphasized in Chart 1. In no other form of cardiac disease is the fatal issue so common in the early decades of life. Indeed in a hospital where for years, there was no large children's ward, nearly 28 per cent of patients showing acute rheumatic endocarditis at necropsy, were under the age of 10; over 72 per cent under 20. One has but to glance at the chart to see how different are the figures in infective endocarditis.

Rheumatic heart disease is essentially subacute leading to chronic valvular disease. Nearly two-thirds of these patients dying with evidences of

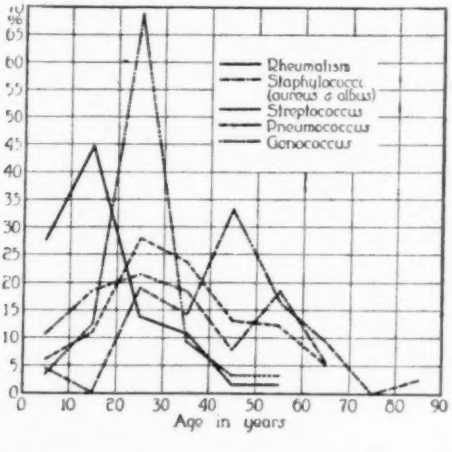

CHART 1. Acute and subacute endocarditis. Age incidence in various infections by decades. (From Edinb. Med. Jr., 1931, n. s., xxxviii, 242.)

acute rheumatic cardiac disease showed clinical or post-mortem evidence of pre-existing chronic valvular changes. Not infrequently where the fatal attack was supposed to be primary, clinical and pathological evidence of previous changes were found, indicating what should be more generally realized, namely that the early rheumatic cardiac changes may steal on the patients like a thief in the night. Often, as Swift especially has pointed out, the fever is moderate or even absent for considerable periods of time and arthritis is trivial or absent. There were long remissions and frequent recurrences. Chills are rare. Embolic phenomena were never observed except in instances of marked myocardial insufficiency, usually in association with auricular fibrillation.

Petechiae are rare in rheumatic endocarditis. In not one of our sixty-five fatal cases were petechiae observed. Anemia as a rule was rather moderate, although there was a fairly well marked leucocytosis averaging between 14,000 and 18,000 per cu. mm., very much like that in subacute infective endocarditis. (Chart 2.) Albuminuria was common at the height of the disease but acute glomerulonephritis, so frequent in infective endocarditis, was not observed. Acute suppurative processes common in some infective endocarditides, were not seen.

Serofibrinous pericarditis is a common and characteristic manifestation of rheumatic cardiac disease. In infective endocarditis it is unusual. Serofibrinous pericarditis is characteristic of rheumatic heart disease and tuberculosis. A glance at Chart 3 in which the frequency of pericarditis in rheumatic heart disease is compared with that in the infective endocarditides is striking. (Unshadowed areas in each column represent adherent pericardium.) Pericarditis in infective endocarditis is not infrequently suppurative; never in rheumatic carditis.

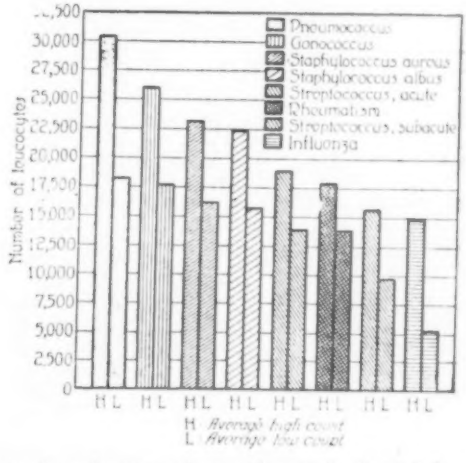

CHART 2. Acute and subacute rheumatic and bacterial endocarditis. Average leucocyte counts—high and low. (From Edinb. Med. Jr., 1931, n. s., xxxviii, 263.)

Streptococcal endocarditis is that form which is most likely to be mistaken for rheumatic heart disease. In 186 instances of streptococcal endocarditis unassociated with acute rheumatic changes serofibrinous pericarditis was observed in little over 4 per cent.

The acute myo- and endocardial changes of rheumatism are anatomically characteristic. The perivascular Aschoff bodies are generally easily to be distinguished from the relatively unimportant areas of round cell infiltration in infective endocarditis. The acute verrucose vegetations on the valves and the roughening and fibrinous exudate in the outer part of the left auricle, so characteristic of rheumatic heart disease, are associated with subjacent intravalvular and subendocardial inflammatory changes which are distinctive.

Rheumatic endocarditis is clearly a reaction to focal subendocardial necrotic and inflammatory changes.

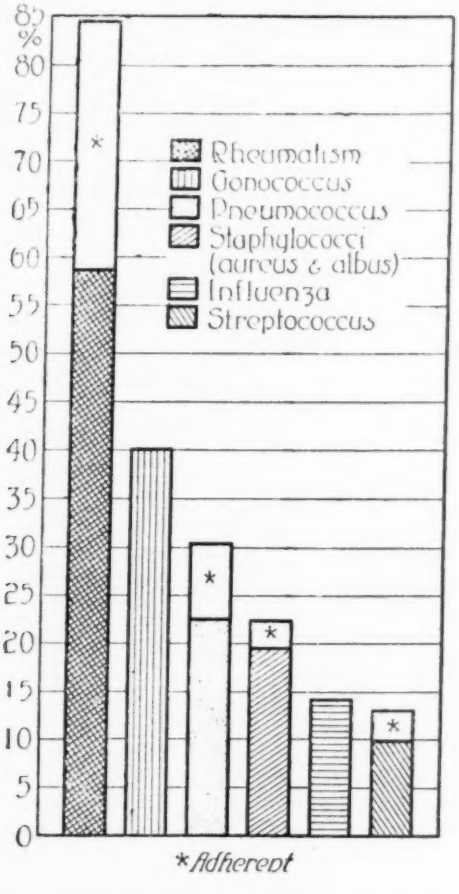

CHART 3. Acute and subacute endocarditis. Relative incidence of pericarditis. (From Edinb. Med. Jr., 1931, n. s., xxxviii. 257.)

The distribution of the valvular lesions in rheumatic heart disease is characteristic. The overwhelming frequency of involvement of the mitral, and secondly, of the aortic valves is apparent in Chart 4 which illustrates the distribution of the valvular lesions in rheumatic endocarditis compared with that in the various infective endocarditides. The relative frequency of tricuspid involvement is interesting but the tricuspid involvement, though common, is usually not extensive and is rarely seen apart from mitral disease. The similarity between the distribution of valvular lesions in rheumatic and streptococcal disease is apparent.

These figures relate only to the distribution of *acute* lesions at necropsy. Among over sixty instances of rheumatic heart disease dead with acute valvular changes, every one showed acute or chronic disease of the mitral valves and 83 per cent of the aortic. Affection of the pulmonic valves is very rare.

Cultures from the circulating blood are usually sterile, an important diagnostic point in doubtful cases. Occasionally, streptococci may be recovered. These are usually non-hemolytic and not found in large numbers or constantly; sometimes only in anaerobic tubes. That there may be exceptions will be mentioned later.

Rheumatic endocarditis, then, is a single feature of a well defined disease picture recognizable usually clinically and anatomically.

The striking characteristics of rheumatic heart disease are its prevalence in early youth, notably in the first two decades; the frequent insidiousness of

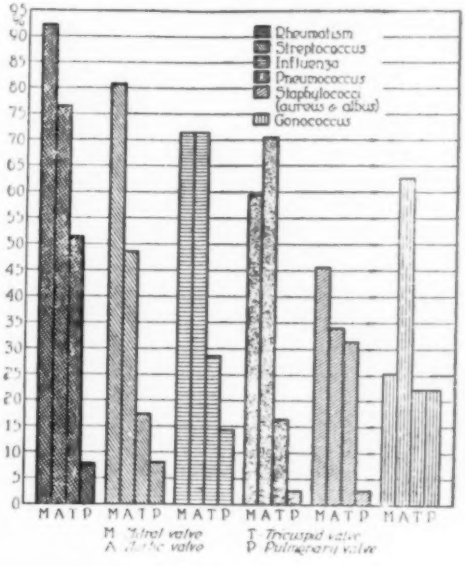

CHART 4. Acute and subacute endocarditis. Proportional involvement of individual valves. (From Edinb. Med. Jr., 1931, n. s., xxxviii, 253.)

its onset and course; its striking tendency to chronicity through recrudescences and recurrences; its evolution into the characteristic chronic valvular heart disease; its common association with fugitive non-suppurative polyarthritis and chorea; the frequency of serofibrinous pericarditis ending in an adherent pericardium; the characteristics and distribution of the valvular, vascular and widespread myocardial changes. It is notable anatomically and pathologically for the circumstance that the non-suppurative serositides, as well as the relatively benign rheumatic endocarditides appear at the outset to be connected with subjacent periarticular, sub-endocardial or subpericardial changes. The process does not originate on the surface.

The most important differential clinical characteristic of rheumatic heart disease is that it leads to death through myocardial failure owing to damage to muscle, valves or pericardium resulting from the immediate effects of acute inflammatory changes or more commonly to the prolonged influence, often largely mechanical, of deformities incident to the scarring of healing lesions. Even in acute rheumatic fever with symptoms of a grave intoxication the fatal issue is usually preceded by myocardial insufficiency with dilatation and congestive failure.

In *infective endocarditis*, on the other hand, the earliest changes take place on the surface of the endocardium appearing as small, soft vegetations packed with bacteria along the lines of contact of the valves. At the base of these vegetations there is necrosis and a spreading inflammatory process which, according to the malignity of the infection and the resistance of the individual, leads to a more or less rapid destruction of the subjacent tissues. Implantation of the infection may follow on spots where the thrombi come in contact with the neighboring heart wall. From the agitated thrombi emboli are commonly distributed by the blood current. These embolic phenomena are among the most characteristic symptoms of infective endocarditis especially of the subacute and chronic forms. Renal embolisms may be so extensive as to result in pain and obvious hematuria or they may be recognized only by occasional showers of red blood corpuscles found microscopically in the urinary sediment. Embolism of the spleen is apparent through the pain and tenderness caused by overlying peritonitis. Cutaneous and subcutaneous embolisms result in phenomena, all the way from tiny petechiae to larger ecchymoses showing a white centre and an hemorrhagic border, or larger swollen cyanotic areas which are very tender. The little tender, cyanotic spots in the pads of the fingers or toes (Osler), and the larger like areas in the soles of the feet and the hands (Janeway), are almost diagnostic*. Small longitudinal painful hemorrhages under the fingernails (Horder) are frequent. Cerebral embolism with hemiplegia is very common, and embolism of larger vessels may result in peripheral gangrene. Mycotic aneurysms are frequent.

*These, as have been pointed out by a number of observers, may be dependent on occlusion of capillaries or smaller vessels by swelling and proliferation of endothelium rather than by embolism.

The character and symptoms of infective endocarditis vary greatly according to its etiology. Infections with *Streptococcus haemolyticus, Pneumococcus* and *Staphylococcus aureus* are notably acute and rapidly fatal; the lesions, ulcerative and destructive. Infections with *Gonococcus* or *Staphylococcus albus* which are rare, although the lesions are almost equally destructive, are somewhat less malignant as a rule and a little less acute in their course. Gonococcal endocarditis ends sometimes in recovery. Endocarditis due to more attenuated streptococci or more rarely to the Pfeiffer bacillus pursues often a subacute or notably chronic course lasting sometimes upwards of a year.

The more acute forms of bacterial endocarditis are not often confused with rheumatic heart disease. The valvular lesions are commonly unrecognizable and excepting in those acute ulcerative affections where there is an extensive destruction of tissue, the phenomena are essentially those of a rapidly fatal acute septicemia hastened generally in pneumococcal infections, by meningitis. It is the more subacute and chronic bacterial endocarditides due, in our series of 121 cases followed to a fatal termination, generally to an attenuated streptococcus (74.1%), gonococcus (10.8%), or Pfeiffer's bacillus (7.5%), which may simulate rheumatic heart disease.

In addition to the embolic phenomena already referred to, these subacute and chronic infective endocarditides have certain characteristic features—the insidious onset; the long, moderate, remittent or intermittent fever, which, indeed, may, for considerable periods of time, be almost absent; the gradually progressive secondary anemia; the leucocytosis of about the same or a little less intensity than that observed in rheumatic heart disease; the splenic enlargement; the Hippocratic fingers; a curious brownish-grey *café au lait* complexion (Libman); the gradual development of a glomerulonephritis, usually regarded as embolic, with the appearance of albumen and red blood corpuscles and casts in the urine, and eventually of edema and evidences of renal insufficiency. Cultures from the blood in a great majority of instances yield non-hemolytic, green-growing streptococci in gradually increasing numbers. Subacute *infective endocarditis is usually fatal* after a period of from a month or two to a year or even more.

The terminal stages are generally those of a grave septicemia. The element of myocardial insufficiency was striking in only a quarter of ninety-nine fatal cases followed to a termination. Auricular fibrillation, not uncommon in rheumatic heart disease, is rare. The distribution of the lesions is very similar to that in rheumatic heart disease, for the simple reason that subacute streptococcal and influenzal endocarditis is found generally (70 per cent of our streptococcal, all of our eight influenzal infections) on valves or mural endocardium the seat of previous rheumatic heart disease.

In two respects subacute and chronic vegetative endocarditis and subacute rheumatic heart disease are similar: (1) The distribution of the lesions, commonest on mitral and aortic valves; (2) the common sub-

acute course. But while in *rheumatic fever* the intoxication as a rule is not very great, the anemia not very pronounced, and embolic phenomena are absent, in *infective endocarditis*, general constitutional symptoms, fatigue, anorexia and progressive anemia are striking and embolic phenomena are common. Osler's phenomena in fingers and toes are almost pathognomonic. Nephritis, rare in rheumatic heart disease, generally appears in infective endocarditis. Splenic enlargement is rare in the former, the rule in the latter. Cultures from the blood are usually sterile in rheumatic heart disease, generally positive in infective endocarditis.

The termination of subacute rheumatic heart disease may be in death from myocardial insufficiency but is usually in recovery with the establishment or aggravation of an already existing chronic valvular lesion. Subacute infective endocarditis is generally fatal, the terminal symptoms being those of a grave septicemia and nephritis. Signs of myocardial failure are usually unimportant.

There are certain exceptions, however, to those rules: (1) *Now and then non-hemolytic streptococci are cultivated from the circulation in rheumatic fever.* Usually positive cultures are only occasional and bacteria are obtained in small numbers. I have seen two instances, however, of rheumatic fever of three or four months' duration in each of which, among a number of negative results there were three positive cultures of streptococcus viridans. In each of these instances, the youth of the patient, 14 in one (Tredway's case*), 19 in the other (Ruffire's case), the absence of embolic phenomena, the lack of a grave general intoxication, the absence of splenic enlargement, even in the presence of repeated positive cultures, led to a correct diagnosis; in each instance the patient recovered. In neither of these cases were the arthritic symptoms important. (2) Recovery from infective endocarditis is probably not altogether so rare as is generally thought. On this Libman especially has insisted. Few pathological anatomists and few clinicians who pass the hours that they should in the pathological laboratory are unfamiliar with the irregularly scarred and deformed valves which could scarcely be due to anything else than past vegetative endocarditis. It is difficult, indeed sometimes impossible, to distinguish convalescence from vegetative endocarditis where the bacteria have disappeared from the blood, from a rheumatic heart disease. This or the absence of positive blood cultures, would certainly have been impossible in Perry's† remarkable instance of gonococcal endocarditis with recovery which I had the good fortune to see on several occasions.

(3) It must be remembered that in rheumatic heart disease with auricular fibrillation extensive peripheral embolisms may follow the dislodging of bits of thrombi in the auricular appendage. Multiple cutaneous, renal

*T. Palmer Tredway: Endocarditis and pericarditis with blood stream infection of *Streptococcus viridans*, Penn. Med. Jr., 1930, xxxiii, 389.

†Perry, M. W.: Gonorrhoeal endocarditis with recovery, Am. Jr. Med. Sc., 1930, clix, 599-605.

and splenic embolisms under such circumstances may, as I have seen, on several occasions, give rise to a rather confusing picture. Diagnosis may indeed be impossible.

(4) Such embolisms may occur in chronic rheumatic heart disease without fibrillation from the formation of mural thrombi in the left auricle. Of this I have seen one striking example.

The distinction between infective and rheumatic endocarditis though usually easy, may be difficult. One should not forget that it may be a delicate question which, like all other clinical problems can rarely be settled by the laboratory alone. It is well to remember that in subacute rheumatic heart disease mural thrombi may form without auricular fibrillation, giving rise to peripheral emboli very suggestive of vegetative endocarditis; that non-hemolytic streptococci may occasionally be obtained from the blood during acute rheumatic carditis, and, now and then, on several occasions; that a diagnosis on the one hand of rheumatic carditis or on the other hand of infective endocarditis cannot be made without a careful consideration of all the evidence; that a fatal prognosis in the absence of immediately threatening symptoms need never be made in either affection.

A Theory of the Causation of Cardiac Pain*

By Alexander Lambert, M.D., *Professor of Clinical Medicine, Cornell University, New York City*

An unsolved problem in medicine stands as a challenge to every physician, and cardiac pain has long stood in this position. It is therefore with peculiar pleasure, and with keen appreciation of the compliment, that I accepted your Chairman's invitation to offer you some heretical opinions concerning its causation.

The most recent reviews of Angina Pectoris by Obendoeffer, Kirch and Edens express the almost universal medical belief that cardiac pain is caused by a spasm of the coronary arteries. But this spasm is an unproven theoretical assumption brought forward years ago by Nothnagel. Huchard collected over sixty explanations of cardiac pain, and in some of these it is even claimed that the pain is due to spasm or anemia of cardiac muscles, forgetting that only stimulation of nerves can produce pain.

The nervous system for the heart and its reflexes belongs to a very ancient mechanism. The heart, unlike the kidneys, does not develop segmentally, but originating in the distal portion of the head descends longitudinally. Its nervous system is derived from the autonomic nervous system, and is obtained from both the sympathetic and cranial portions.

The efferent nerves to the heart are derived from the vagal as well as the sympathetic system, but the afferent sensory nerves belong only to the sympathetic portion. The cardiac vagal system does not carry fibers for pain, its afferent nerves carrying depressor and other vasomotor fibers. The afferent sensory fibers, passing chiefly through the stellate ganglia, join by the rami communicantes the posterior spinal nerve roots, and traversing their ganglions to the spinal cord pass upward by the spinothalamic tract through the midbrain to the centers for the autonomic nervous system in the hypothalamus in the caudate end of the diencephalon.

To appreciate clearly the ancient reflex mechanism controlling the heart, and through the break down of which pain is produced, it is necessary to review briefly some of the physiology of the autonomic nervous system, and that is best done by quoting Cannon's interpretation of it. In general the cerebrospinal nervous system furnishes the discriminative consciousness localizing internal sensation or external danger, and presiding over the action of the skeletal muscular system, makes and carries out the choice of fight or flight. Through the action

*Presented at the Baltimore meeting of the American College of Physicians, March 23, 1931.

of the autonomic nervous system, on the other hand, are furnished to the cerebrospinal nervous system, and skeletal muscles the supplies of sugar, oxygen and adrenal energy sufficient to maintain successfully the choice to fight or flee.

The sympathetic portion of this system differs from the cranial and sacral portions, in that the outlying ganglia are so placed in the sympathetic portion that the nerves going through them give fibers to each successive ganglion before the nerve is finally distributed to the viscera. The cranial and sacral systems however, have their outlying ganglia in the viscera themselves. This, as Cannon points out, produces a generalized effect over all the viscera in any sympathetic discharge, while in cranial and sacral discharges of energy the stimulation can easily go to a single viscus to perform a special function without involving any other viscus. As for example, a rise of blood pressure from the general sympathetic stimulation involving the whole splanchnic system, produces a general bodily effect: while the stimulation of the cranial portion to increase the tone of the intestines does not simultaneously slow the heart.

Moreover, in those viscera to which two portions of the autonomic system are distributed, the action between the sympathetic and the cranial, or sacral portions are in opposition to each other. For example, in the heart the sympathetic fibers are the accelerators and the dilators of the blood vessels, while the cranial or vagal fibers are the inhibitors of the heart action, and the constrictors of the blood vessels, and this interchange of opposing action produces the even functioning of the heart and its instantaneous reply to varying demands for increased output.

In general it may be said of the three divisions of the autonomic nervous system that the cranial takes part with the sympathetic in the functions of respiration, circulation, digestion and absorption; the sacral portion with the sympathetic controls the elimination of the waste of the body, through emptying of bladder and rectum and those functions included in racial continuation.

The sympathetic portion secures by its general reactions the delicate balance of the body between its internal and external relations, that is, to use Cannon's phrase, in preserving the homeostasis of the body. Through its special hormone, adrenin from the adrenal glands, the sympathetic system increases and prolongs its own action.

Through this sympathetico-adrenal action the heat loss and heat production of the body is regulated, and the evenness of the bodily temperature is preserved. Through this mechanism the acid-base equilibrium is maintained, and the blood sugar for muscular exertion is prevented from falling to a dangerous degree. The circulatory adjustments, constriction of the splanchnic vessels with rise of blood pressure, acceleration of the heart, discharge of extra corpuscles from the spleen, with increased distribution of extra oxygen, and facilitation of the respiratory processes are all made by means of the sympathetico-adrenal system. Besides these physical and chemical ad-

justments, there are some nervous reflexes involving the sympathetico-adrenal system, which react intensely on the heart and general circulation. Bard has demonstrated that the center of the autonomic nervous system is located in the ventral portion of the caudate end of the hypothalamus.

Animals with their cerebral cortex removed, but with the hypothalamic center intact, still react with purposeful actions, and show prolonged periods of sham rage to slight irritations. It is evidence of emotional reaction with all inhibitions from the cortical centers removed, and the physical symptoms as in cats, of the bristling of their hair over the entire body and tail, their growling, snarling, spitting, anger, and clawing and endeavoring to scratch and run away, often with defecation and micturition, show the intensity of the general discharge from the sympathetic system. It is the evident counterpart of the blind rage of the human young in their fighting, biting, shrieking anger from a loss of cortical control. These are excellent examples of the discharge from the central nervous center, through the sympathetic system to its peripheral effectors, the skeletal muscles and viscera.

Cannon has conclusively demonstrated that any high degree of excitation in the central nervous system, whether felt as anger, terror, pain, anxiety, joy, grief or deep disgust, may rouse the sympathetic system to activity, and affect in a stereotyped fashion the functions of organs which that system innervates.

Many of the reflexes of angina pectoris and cardiac pain occur through this neural mechanism, the attacks of angina pectoris being particularly susceptible to emotional origin.

Beginning with the cardiac reflexes in the early stage of muscular exercise, it is the sudden exertion, as walking against the wind, or up a slight grade, which is often the earliest occurrence to inform a patient that his heart can give him pain. Probably the first reflex action from exertion is the increased depth and rapidity of respiration, and this is followed by a conscious reflex from the higher nervous centers, which quickens and deepens the respiratory flow. This starts the necessary supply of increased oxygen, and with the bellows effect of the chest, increases the venous flow into the heart as the skeletal muscles add their increase of blood, going to the heart through the large veins. There is a rise of capillary and venous pressure, and the Bainbridge reflex occurs in the right auricle; i.e., as the increased venous blood distends the auricle, the vagus nerves around the great veins are inhibited and the accelerators are stimulated so that the rate of the heart increases in proportion to the venous return, and the blood is hurried on through heart. The increase of CO_2 and the lack of O_2 also accelerate the heart.

The anoxemia greatly increases the coronary flow. With the general muscular exertion there is an inhibition of the splanchnic area, and a general rise of arterial blood pressure in the body. As blood pours into the ventricles, there is a stretching of the myocardial muscles, with an increased output per

beat of the heart. Both the rise of aortic pressure, and the increased cardiac output greatly increase the coronary flow through the action of Anrep and Segal's coronary reflex, which is a reflex diminution of tone of the vagal vasoconstrictor fibers producing an increased coronary flow. The rise of CO_2 tension and the H-ion concentration of the blood also add to the increase of the coronary circulation. In normal vigorous cardiac contraction the coronary vessels are filled and emptied with each contraction of the heart, and during each beat of the heart the coronary flow varies practically between empty vessels and well-filled flowing circulation. The inflow into the coronary vessels occurs only during the diastolic period, being practically stopped in vigorous healthy hearts during the systolic compression of the vessels by the myocardium. These physiologic details are probably tedious to you, but their definite picture is necessary to appreciate the cause of cardiac pain, because it is through the breakdown of the normal physiologic processes that cardiac pain is produced.

It is important to remember that the blood supply of the first portion of the aorta is only from both coronaries which form the vasa vasorum of this portion of the aorta, so that the blood supply of the ascending portion of the aorta and of the heart is from the same vessels.

Spiegel and Wasserman have shown definitely that the pain from the aorta follows the same pathways as pain from the heart.

Singer has demonstrated that eradication of both stellate ganglia makes insensitive all cardiac and aortic tissues as far as the left subclavian artery.

Dogiel demonstrated that the sensory nerve endings of the coronaries and of the aorta and of the blood vessels in general, lie in their adventitial coat.

Odermatt in studying the sensitiveness of blood vessels has clearly shown that some arteries are sensitive to ligation, and small arteries more so than large ones.

Bazett and McGlone have shown that puncture of the radial is more painful than that of the brachial, and that the pain is a dull aching generalized pain, difficult to locate, and difficult to bear, causing a sudden sensation of warmth with profuse sweating, sometimes accompanied by nausea, and in some individuals by a desire to defecate, and often followed by coldness, faintness and actual loss of consciousness.

Odermatt found also that arteries that are sensitive to ligation are also sensitive when their adventitia is stretched or distended, that is, the stretching or distension of these same arteries produces pain, and it is by distension and not by contraction that pain arises.

Spiegel and Wasserman have shown also that stretching of the aorta produces intense pain.

Singer has demonstrated that an acute ischemia of the cardiac muscle is without any painful reaction in the experimental animal, and that the endocardium and cardiac muscle are completely refractory towards chemical, mechanical and Faradic irritation. The pericardium and epicardium are definitely sensitive to mechanical and

chemical irritation, but Faradic irritation provokes little or no reaction. The sensibility of the coronary vessels is dependent on the intactness of the adventitia, which possesses a strong mechanical and chemical sensibility. The aorta is always but feebly sensitive to Faradic irritation; it is only mildly sensitive to chemical inflammatory irritations, but to mechanical pinching and pulling and stretching, the aorta is strongly sensitive. Here also the sensibility depends on the anatomical intactness of the aortic adventitia, but sensitiveness to pain on the part of the media and intima of the aorta could not be demonstrated.

Clinically we are aware that sudden rises of blood pressure may be accompanied or followed by an attack of cardiac pain. Cardiac pain is, however, not dependent alone on blood pressure, for pain occurs with low blood pressures, or with high blood pressures, and Bayliss has definitely stated that the stimulation of any afferent nerve, except the depressor nerve of the heart, will cause this rise of blood pressure. The depressor nerve rises from the heart and aorta, and passes up to the vagus. There is a good deal of discussion as to whether or not this is present in human beings, but the work of Vitti shows definitely that in the majority of mankind this nerve is present, and passes upward separately or in the main stem of the vagus to the superior laryngeal nerve. Its function is to regulate the blood pressure by bringing about a general fall of pressure, and to reduce the blood pressure when it rises to too great a height.

Clinically cardiac pain arises after the period of healthy athletic youth has passed, and the degenerations of senescence have begun, when the heart and its vascular system have become permanently damaged, when the heart has lost its power of instant vigorous response, and its ability to regain its normal functional vigor. It is in this period of senescence in the fifties and sixties that angina usually occurs. If it occurs earlier, it is through premature disease of its tissues, and the inability of its normal reflexes to bring about the normal action and equilibrium between its muscular function, and its own vascular supply.

As the myocardium degenerates there is an increasing dyspnea on exertion, and there finally comes a time when the degenerated myocardium can not contract with adequate vigor to drive on the increasing blood coming into the heart from exertion. The myocardial muscles stretch to increase the output per beat, but can not contract with sufficient vigor to accomplish it. For a while an increased heart rate per minute may act as a substitute for increased output per beat, but there comes a time when the lack of output per beat ceases to stimulate the reflex to cause increased coronary flow, and the heart is in the condition of dependence for its coronary flow on increase of blood pressure. The degenerated muscle cannot contract vigorously enough to empty out the heart, nor clean out its own coronaries. With the incompetent cardiac muscle there occurs an increasing vascular congestion, and finally dilatation of the coronary arteries by which stretching of the adventitia is

produced from over distension of the diseased arteries, and pain is the result. This pain arises from stimulation of the afferent nerve endings in the adventitia of the coronary arteries, and the pain persists until the coronary circulation can recover itself through increased muscular action of the myocardium, or diminished inflow of blood into the heart brings relief.

When the pain arises from the first portion of the aorta, the mechanism of its causation is different. With an aortitis and diseased aortic wall, or with inflammatory processes around the vasa vasorum of the adventitia which press on the sensory nerve endings, any sudden increase of blood pressure in the aorta which some emotion may cause, which any sudden demand for increased cardiac action will produce, will cause an increased stretching of the aortic adventitia sufficient to produce pain, but not sufficient to cause reflex action of the depressor nerve to occur, and by lowering of blood pressure bring about a cessation of the stretching of the adventitia. The giving of the nitrites instantly produces a general fall of pressure, a general relaxation of the vascular muscularis, and the painful stretching ceases. The action of the nitrites is substituted for that of the depressor nerve.

Clinically in attacks of angina pectoris the pain is accompanied with symptoms from widespread reflexes. There is at times lacrimation, salivation, pupillary dilatation, general intense sweating, nausea, and vomiting, or intense belching of gas. There is not infrequently a desire to micturate, and Olser and others report testicular pain. The observations of Bazett and McGlome already quoted, demonstrate that the aching pain from arterial puncture is often followed by similar reflexes, such as a sudden sensation of warmth followed by sweating, and then coldness, faintness and even loss of consciousness. In some individuals there may be nausea at times, and a desire to defecate.

The analogy of the clinical picture of certain attacks of coronary thrombosis and the sequence of reflexes from arterial puncture is apparent. It would also seem to indicate that the pain of angina, as well as of coronary thrombosis, is of vascular origin originating in the afferent nerves of blood vessels, passing to the general autonomic center in the hypothalamus. The intensity of the pain causes an intense general sympathetic discharge producing a reflex action in both the cranial and sacral portions of the autonomic system. The pain simultaneously manifests itself through the afferent connections of the sympathetic system with the cerebrospinal nerves, being felt and localized in cortical consciousness as present in the familiar positions on the trunk and down the left arm. These widespread reflexes produced by the diffused discharge of the sympathetic system indicate how ancient is the mechanism of the cardiac pain, and to explain it satisfactorily we must consider the nervous mechanism of the heart before the neopallium was present.

The theory here offered is further supported by the results from the operations of sympathectomy performed to eradicate the pain in angina, or the occurrence of the whole anginal

symptom complex. Hesse reviewing 135 cases of various methods of sympathectomy, concludes that extirpation of the superior cervical ganglion was successful in 62.57 per cent but cutting across the superior cervical ganglion just above the origin of the great cardiac nerve, and removing the cervical sympathetic cord to just above the inferior cervical ganglion, gave 80 per cent of successes. Removing the cervical chain of ganglia with the stellate ganglion was successful in only 56 per cent. Cutting off the pathway for the vasomotor reflexes in the superior cervical ganglion is therefore more successful than obliterating the afferent and accelerator fibers through the stellate ganglion. The most successful operation obliterates the vasomotor pathway, plus some of the afferent fibers, passing through the middle sympathetic nerve and ganglion, and prevents the reflex action of the general sympathetic discharge from culminating in an attack of angina.

How does this theory of vascular distension instead of vascular contracting spasm explain better the puzzling clinical manifestation of cardiac pain? Cardiac pain is brought about by increased muscular exertion as we have just shown. It is also produced by going into a cold room or getting in between cold sheets. Cold produces contracting of the skin vessels, a sudden increase of blood pressure, a stimulation of the sympathetico-adrenal action with adrenin secretion and acceleration of the heart action with quickening of the metabolism to increase heat production. Cold therefore produces increased cardiac demands for which the myocardial muscles may be inadequate, and pain occurs as above.

In pernicious anemia, or in other severe anemic conditions, cardiac pain sometimes occurs. In anemia the coronary circulation is at times increased five fold above normal, but the myocardial muscles suffer in their nutrition. The diseased coronaries are already distended with blood, and with an inadequate myocardial contraction pain is all the more quickly produced. But following blood transfusion the pain ceases, because the coronary flow returns to normal proportions and with a better nourished myocardium, improved in the vigor of its contraction, the coronary distension ceases, and cardiac pain disappears.

Following acute infectious diseases such as influenza there is an acute myocardial degeneration in a subject with diseased coronaries, and there is an acute myocardial breakdown producing the coronary distensions and pain.

The cardiac pain following nicotine intoxication apparently arises from paralysis of the synapses between the preganglionic sympathetic fibers and the postganglionic fibers in the sympathetic ganglia.

Woolhard has brought forward evidence showing that the sympathetic nerve fibers alone supply the ventricular muscles. The sympathetic accelerators influence the conductility of the cardiac impulse and the contractility of the muscles. When the nicotine poisoning is sufficiently intense there is paralysis of the accelerators which produces the same inadequate myocardial contraction as degeneration of the muscle. When the nicotine is removed the pain ceases. The use

of tobacco in some patients increases the frequency and intensity of the anginal attacks, as the accelerator paralysis is added to the already existing myocardial degeneration.

Anger, fear, joy or pain, or any intense emotion, causes, as we have seen, an intense general sympathetic discharge from the hypothalamic autonomic center, and causes, as Cannon has shown, a secretion of adrenin and increased blood pressure and acceleration of the heart's action, which may make increased demands on an inadequately contracting myocardium, with the cycle of events as already described bringing on the undue stretching of the aorta, or the distension of the coronaries and cardiac pain.

In coronary thrombosis or infarction the pain can be produced either by causing inadequate myocardial contraction, or by causing coronary distension in the obstructed blood vessel proximal to the obstruction. If there is sufficient collateral circulation in the coronaries to prevent the vascular distension, pain would not occur.

The theory of cardiac pain here presented seems also to explain the incongruous pathologic anatomy found in post mortem examinations of those patients dying in an attack of angina pectoris, or those who gave a history of having suffered cardiac pain. Aortitis, especially luetic aortitis, has been found with a history of previous pain, and frequently found with a history of no pain. Coronary arteriosclerosis with distended vessels, or with thickened and occluded arteries, and with or without calcification, has been found with histories of pain and anginal attacks, and also with definite histories of no pain. Coronary thrombosis and infarct occur also with and without pain. Aortitis with or without coronary disease and coronary disease with normal aorta has caused many discussions of the causation of cardiac pain.

Luetic aortitis, beginning as it does in the vasa vasorum, more frequently seems to cause pain than aortitis from other causes. Kutchera Aichbergen emphasizes the fact that a history of pain is more frequently present with thin walled dilated coronary arteries than with the thickened or calcified vessels. The observation of the writer during the past two years seems to corroborate this opinion. Whatever the cause of arteriosclerosis, the first tissue to degenerate is the internal elastic layer which causes a strain on the muscularis, and a distension of the vessel. As Thoma showed, the thickened intima is a defense reaction to prevent the vascular distension, and to protect the muscularis. Cardiac pain occurs chiefly in the early years of senescence when the arterial degeneration has actively begun in both blood vessels and myocardium, and does not wait till the calcified processes of senility have occurred.

It seems, therefore, judging from the evidence of experimental work, that cardiac pain arises in the ancient mechanism of the autonomic system originating in the sensory nerve endings of the cardiac vascular system, and in the wall of the adjacent aorta. This pain occurs when there is an abnormal distension of the adventitial coats of the aorta and coronaries, through the breakdown of reflex mechanisms to which the degenerated tissues of the aorta and myocardium are unable to respond effectively.

The Insulin Coefficient, an Improved Method for the Clinical Control of Diabetes Mellitus*

By JOHN R. WILLIAMS, M.D., F.A.C.P., *Rochester, N.Y.*

THE diagnosis and treatment of diabetes are as yet on an unsatisfactory basis. In advanced cases the diagnosis is easy but in the border-line and doubtful groups a clinical problem is presented which is very difficult of solution. The finding of sugar in the urine to a large group of physicians is prima facie evidence of diabetes, although it has been clearly established that sugar and other reducing substances may be found in the urine in a number of conditions other than diabetes.

With the advent of blood chemical methods a few years ago, blood sugar assumed high importance in the diagnosis of the disease. To many physicians a high blood sugar is pathognomonic of diabetes. Adaptations of blood and urine sugar tests such as the glucose tolerance tests have been developed. These examinations as usually carried out are fraught with possibilities for serious error, harm and injustice to the patient. Every year thousands of persons are condemned to a life of dietary restriction and insulin therapy because in a casual examination of the urine a reducing substance or a sugar has been found which has no disease significance. Numbers of applicants are unfairly denied life insurance for the same reason. It is true that uncontrolled diabetics usually have a glucosuria and high blood sugars, that they also exhibit an abnormal reaction to the glucose tolerance test, but it is also true that a large number of people who have not diabetes will, on occasions, show these same phenomena to a degree which is both disconcerting and confusing. It may be said, therefore, that the prevailing criteria for the diagnosis of diabetes are not very satisfactory.

For similar reasons the guides to treatment which are employed are open to question:

Prevailing Criteria of Treatment in Various Diabetic Clinics

1. Fasting blood sugars.
2. Blood sugars without reference to time of food or insulin therapy.
3. Reducing substances in the urine.
4. Grams of glucose per unit of insulin administered.
5. Normal fasting blood sugar and sugar free urines.

*Presented at the Baltimore meeting of the American College of Physicians, March 24, 1931.

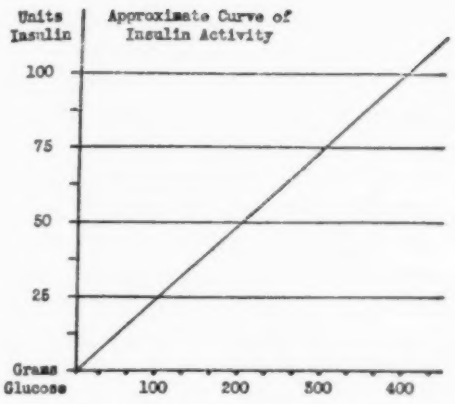

CHART 1

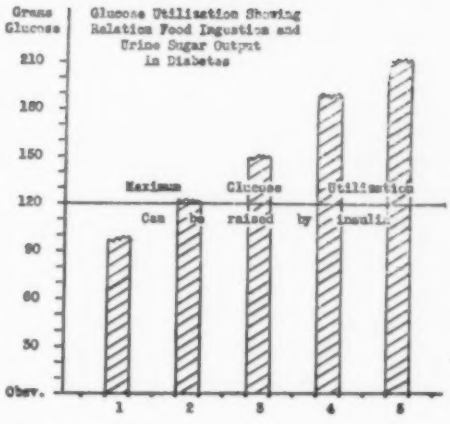

CHART 2

CHART 1. Graph showing approximate curve of insulin activity. The true curve is probably not a linear one, particularly with large amounts of insulin. Within the range of usual clinical application the curve is sufficiently accurate.

CHART 2. Each diabetic patient has a limited capacity to metabolize glucose. Glucose eaten in excess of that amount is eliminated in the urine. There is a fairly definite relation between intake and outgo. Unutilized glucose may be stored for several days before it is eliminated, therefore clinical observations based on single tests may be inaccurate. In this case it is assumed that the patient cannot utilize more than 120 grams. All above that amount is eliminated as urine sugar.

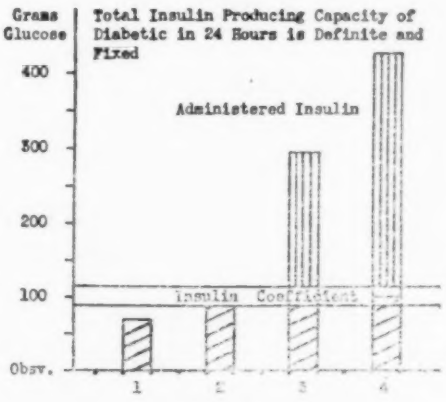

CHART 3

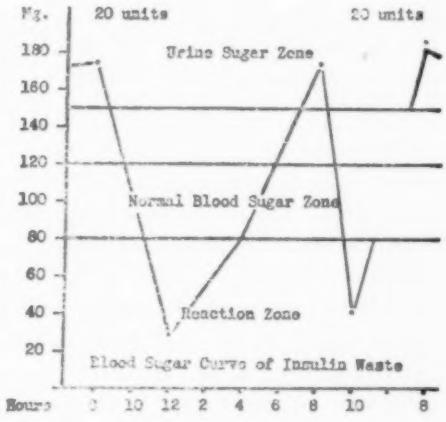

CHART 4

CHART 3. The insulin coefficient in each diabetic is fixed and constant. It cannot be increased by therapy. The ability to utilize glucose can be increased by the supplementary administration of insulin. In this suppositious case the patient is able to utilize only about 120 grams of glucose but when insulin is administered his utilization may be increased to 400 grams.

CHART 4. Blood sugar curve of a diabetic who received two doses of 20 units of insulin daily. Preceding the morning dose he would have sugar in the urine, two hours after it he would have reactions. This phenomenon was repeated in the evening. Insulin dosage which drives the blood sugar down into the reaction zone is wasted.

The blood sugar is a marked variable. While it is usually high in severe diabetes, in many cases it is often low; conversely in mild diabetes it is sometimes high. More important is the fact, which is rarely recognized, that blood sugar is merely a measure of insulin concentration or activity in the blood at the time when the specimen is removed. It is a fluctuating factor and not a constant one as is commonly assumed. Because the blood sugar is high at one hour does not necessarily mean that it will be high all day. One cannot determine the amount of food a patient can utilize in a day by estimating the blood sugar. That information must be gotten in another way, yet it is a common practice for physicians to base their dietary and insulin prescriptions on such data. In short, the blood sugar reveals the intensity of insulin in the blood at a certain time and gives information as to the balance between the previous meal and insulin activity. For this purpose it is valuable.

Qualitative tests of the urine for sugar with copper solutions is another procedure of questionable value. Some of the reagents in common use are so sensitive that they react to other reducing agents than sugar. Even when sugar is present the test is too crude to be of great service. I have seen many patients who have been instructed to follow a program of diet reduction and to increase insulin dosage until the urine became free of reducing substances to these tests. Many of these cases have not had diabetes. "Grams of glucose per unit of insulin administered" is a step in the right direction but it represents a combination of factors and does not take into consideration the insulin produced by the patient. Furthermore it creates the impression that the trouble with the diabetic is that he is not able to properly use insulin and that insulin has a variable strength in different individuals, whereas it is well known that diabetes is due to a failure of the pancreas to make insulin in proper amounts and that insulin has a fairly constant strength and so may be standardized.

"Normal fasting blood sugar and sugar free urine" as a guide to therapy are also open to criticism for reasons which have already been stated and also because, as usually employed, they may be very misleading and are not sufficiently definite. The wide use of this procedure as a guide to treatment undoubtedly has much to do with the great variety of dietary procedures in vogue.

Prevailing Methods of Treatment

1. Underfeeding. Low fat. Insulin only to advanced cases.
2. High fat. Insulin only to advanced cases.
3. Balanced slightly restricted diet. Diabetic foods. Restricted insulin dosage.
4. Diet high in carbohydrates and calories. Heavy insulin dosage.

That patients do fairly well on all these widely varying and opposing procedures indicates a great degree of adaptability in the diabetic.

This conflict of opinion and method, both in the diagnosis and treatment of diabetes, suggests to the critical student that more definite methods of diagnosis are desirable and that while

many plans of treatment are useful there is probably one which may be regarded as the optimum. A solution of the problem may be approached by first defining it. The following statements about the disease are quite generally accepted as facts:

Diabetes is due to a failure of the insulin function of the pancreas.

There is a direct relation between the amount of insulin produced and the severity of the diabetes.

The amount of insulin that an established case of diabetes can produce is quite definitely fixed.

If these statements be true, why is not the correct diagnostic procedure to measure the insulin producing function of the pancreas? And if this be done, why is not the amount of insulin the patient is able to make an index of the severity of the diabetic process and a useful guide to treatment? I believe it can be done and that it is a thoroughly practical method of study. It has been employed in our clinic for three years with very satisfactory results. For its successful application it is first necessary to set forth certain

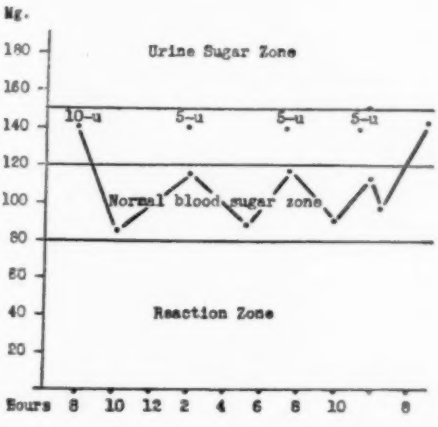

CHART 5

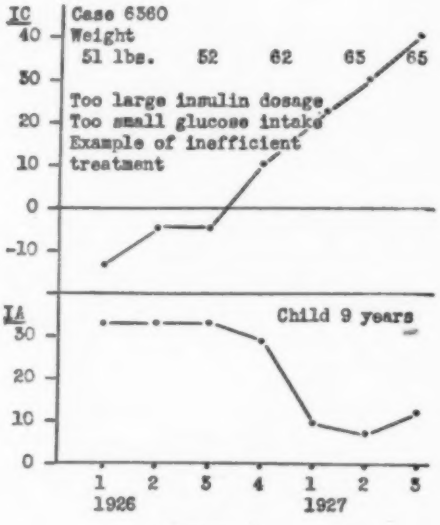

CHART 6

CHART 5. Blood sugar curve of a patient shown in Chart 4. When the insulin dose was reduced, divided into smaller doses and properly spaces, both the glycosuria and the reactions stopped. There was a sharp rise of 15 units in the insulin coefficient. Diabetic patients frequently are greatly helped by rearrangement of the diet and insulin therapy, as in this case.

CHART 6. Showing insulin coefficient graph of improper treatment of a child. This patient carried a persistently high blood sugar and in the endeavor to reduce it the diet was lowered and the insulin dose increased to the point where the coefficient dropped to minus 14. In other words, the patient was wasting a large amount of the insulin that was administered as well as that which he was able himself to produce. He was miserable from reactions and undernourishment. When his diet was corrected and his insulin dose greatly reduced and adjusted, his coefficient rose to 40. This is not an unusual experience with children. The blood sugar is a very unreliable guide to the total glucose metabolism of diabetes.

principles of the metabolism of the diabetic.

The ability of the diabetic to utilize glucose is fairly constant but slowly declines over a period of months or years. It cannot be increased by eating more food. Insulin therapy increases it. Glucose, in excess of the capacity of the body to utilize it, is excreted as urine sugar. For a few days at a time it may be stored in excessive amounts. For purposes of clinical study it should be assumed that the body derives glucose from all foods. In our clinic the standard method of approximating the glucose content of the diet is employed.

100 grams carbohydrate yields 100 grams glucose
100 grams protein yields 58 grams glucose
100 grams fat yields 10 grams glucose

Therefore, the glucose content of the diet for twenty-four hours, less the glucose content of the urine for the same period, equals the amount of glucose stored or utilized. If the observations cover a period of five or six days a fairly accurate measure

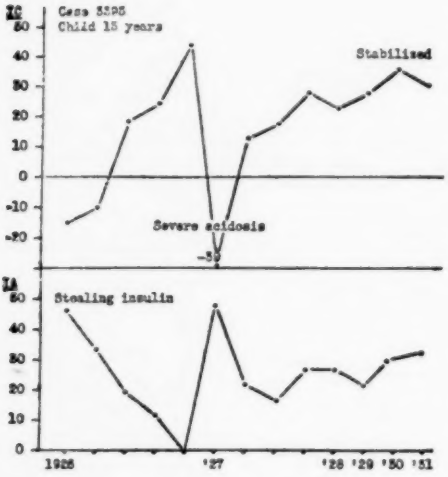

CHART 7

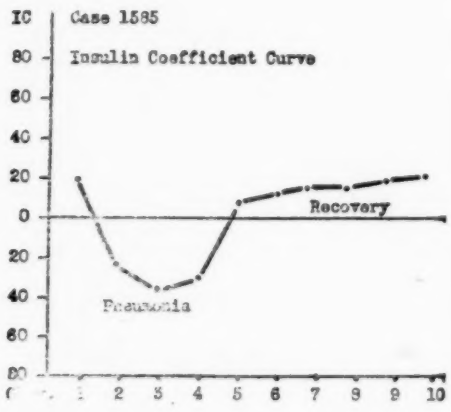

CHART 8

CHART 7. This group shows the insulin coefficient record of a child who began by stealing food. When he was apprehended he tried to conceal it by surreptitiously taking insulin. Several syringes and ampoules of insulin were found secreted in his clothing and room. By supplementing the extra food with insulin he made it appear to us that he was rapidly improving and that less insulin and more food was required. It will be noted that his coefficient rose from minus 15 to plus 45, an astonishing recovery. Accordingly the insulin dose was gradually reduced to the point where it was thought it was no longer needed. At this time his clandestine actions were discovered and effectually stopped by putting him in the hospital under strict observation. The sudden deprivation plunged the patient into coma. Since then he has been co-operative and for three years has been stabilized with an insulin coefficient approximating thirty.

CHART 8. This patient was taken acutely ill with lobar pneumonia. Before the onset of the infection he had an insulin coefficient of approximately 20. He was therefore a severe diabetic but was so adjusted as to be practically well. With the onset of the pneumonia his coefficient rapidly dropped to minus 25, which means that larger doses of insulin given to him, for reasons unknown, were not effective. The action of the insulin was neutralized or partly destroyed, hence the minus coefficient. The fifth observation was made on the day the fever terminated by crisis, the coefficient rising to plus 5. Thereafter recovery was speedy and the index rose to its former level of 20.

of the ability of the body unaided to utilize glucose will be afforded. The foregoing is essentially accurate if the amount of food ingested is not greatly in excess of the capacity of the patient to metabolize it. Therefore, the first step in the problem is to determine the glucose utilization.

The chief action of insulin is the formation of glycogen from dextrose. One unit of insulin promotes the utilization of approximately four grams of glucose. It is commonly stated in the literature of the manufacturers of insulin and also by most authors that one unit of insulin will burn 1.5 to 2 grams of glucose in the body. For several years, in fact, since insulin has been available for clinical use we have made on highly trained, carefully controlled diabetic patients, clinical assays of the product which have been checked by independent animal experiment or assay in another laboratory. Our results almost invariably agree. It may be said, therefore, with confidence, that in the uncomplicated well controlled diabetic one

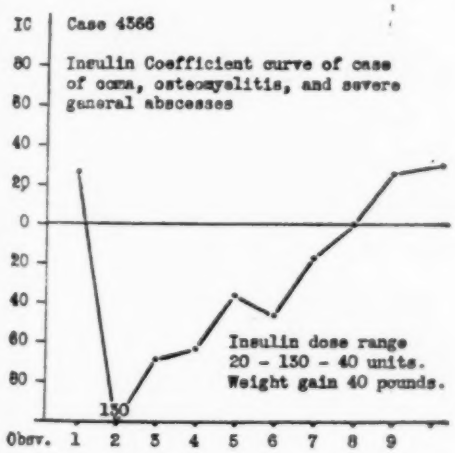

CHART 9

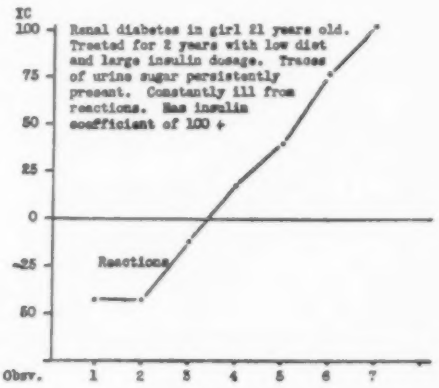
IC
100
75
50
25
0
-25
50
Renal diabetes in girl 21 years old. Treated for 2 years with low diet and large insulin dosage. Traces of urine sugar persistently present. Constantly ill from reactions. Has insulin coefficient of 100 +
Reactions
Obsv. 1 2 3 4 5 6 7

CHART 10

CHART 9. This patient, a male of 28 years, is a severe diabetic with an insulin coefficient of approximately 25. Was taken acutely ill with abscesses and osteomyelitis involving the leg. He was admitted to the hospital in profound coma. 130 units of insulin on the day of admission apparently had little effect on his diabetes. He had a coefficient of minus 130. For several weeks he suffered from large abscesses in various parts of his body. The osteomyelitis in the leg became so severe that death seemed inevitable. Leg amputation was repeatedly urged by counsel. A slowing rising insulin coefficient suggested that the infective disease process was being overcome so operation was deferred. Shortly thereafter the patient made a most miraculous recovery, justifying our faith in the method. The patient within a period of six weeks gained forty pounds in body weight.

CHART 10. Insulin coefficient graph of a renal diabetic. This peculiar disturbance is frequently treated by strict diets and insulin therapy with distinct harm to the patient. Because traces of sugar were frequently found in the urine for two years this patient was subjected to a rigorous diet and excessive insulin therapy. She was confined to bed for weeks constantly ill from reactions which took the form of a mental disturbance. With discontinuance of the insulin and proper arrangement of diet, the patient's coefficient rose from minus 40 to over 100. In a few weeks she was completely restored to health and has remained so over a period of two years. The writer has seen two cases where mild mental disturbance was directly ascribable to insulin reactions.

unit of insulin promotes the utilization of four grams of glucose. It is not claimed that the function of insulin action follows a linear curve. In all probability it does not. With very large doses the ratio of activity declines, but within the range of clinical application and under ordinary conditions it is approximately accurate.

The maximum amount of insulin which a patient may produce in twenty-four hours is designated as the insulin coefficient. In uncomplicated diabetes it is fairly fixed. After a permanent diabetic state is established it rarely fluctuates more than five units. From year to year in well controlled cases it shows very little change.

Example of Test Case

Diet glucose	160 grams
Urine glucose	40 grams
Glucose utilization	120 grams

$\frac{120}{4} = 30$ units insulin required.

After studying several hundred patients in this manner the following classification was made on the basis of severity of the diabetic process:

Insulin Coefficient of	
Normal individual	100 +
Borderline diabetic	75 —
Mild diabetic	40 to 75
Moderately severe	25 to 40
Severe	20 or less

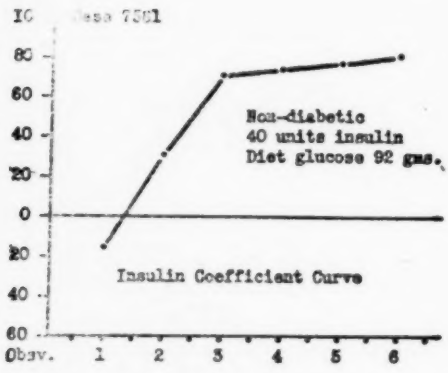

CHART 11

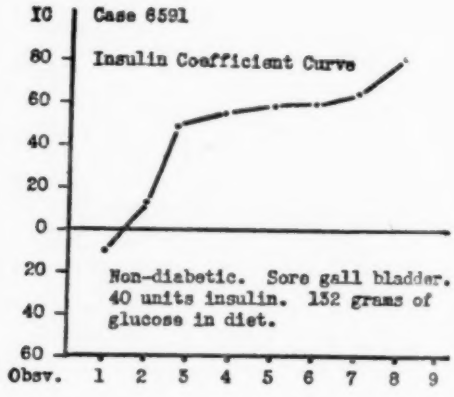

CHART 12

CHART 11. Non-diabetic suffering from a mild psychoneurosis associated with the menopause. Treated for several months on a low diet and large doses of insulin. Erroneous diagnosis based on the occasional finding of a reducing substance in the urine which had no relation to carbohydrate metabolism. Patient was instructed to increase her insulin dose gradually until the urine became clear. Suffered constantly from reactions. Her insulin coefficient under proper dietary regulation rose from minus 15 to over 100 when the tests were discontinued.

CHART 12. This is the insulin coefficient graph of a non-diabetic with a mild gall bladder disturbance. The patient was treated for one year in an institution on a low diet and large doses of insulin. She suffered constantly from reactions. She has a coefficient above 100. The erroneous diagnosis was based on the occasional finding of a reducing substance in the urine and a questionable blood sugar determination. It will be observed that with proper arrangement of her diet, her coefficient rose from minus 10 to approximately 100. Indeed, the maximum was not reached because of the unwillingness of the patient to eat the excessive food required for the test.

The average normal individual eats a diet which will yield from three hundred to four hundred or more grams of glucose. The amount will vary with the eating habits. The diet of the average temperate eater which will include sugar, bread, cake, fruit, and the common vegetables rich in starch will yield about three hundred grams of glucose. The border-line diabetic who practices little dietary restriction and who is difficult to diagnose usually eats about this amount of food. Such a diet would require seventy-five units of insulin. An individual whose coefficient is less than seventy-five should be regarded as a diabetic. Yet for purposes of diagnosis it is often desirable to carry the diet up to the point where 100 units would be required. It is confidently believed that examinations of this sort, carried on over a period of days or even weeks, in which the insulin coefficient of the individual is carefully determined, is infinitely more accurate and valuable than such unnatural tests as the glucose tolerance, or the taking of sporadic blood and urine tests after special meals. In this connection the fundamental definition of diabetes should be borne in mind. It is a disease in which the ability of the body to utilize glucose is partly lost due to a failure of the pancreas to make insulin in sufficient amount. It is not necessarily a disease of high blood sugar or urine sugar. These are incidental phenomena which commonly occur in diabetes but, also, in other maladies. The real tests are glucose utilization and insulin production.

For purposes of work in our clinic we use the following symbols:

Glucose utilization = GU
Insulin required = IR
Insulin administered = IA
Insulin coefficient = IC

$$\frac{GU}{4} = IR$$

$$IR - IA = IC$$

An example of a supposititious case would be as follows:

Glucose utilization = 120 grams
Insulin administered = 10 units

$$\frac{120}{4} = 30 \text{ IR (insulin required)}$$

$$30 - 10 = 20 \text{ IC (insulin coefficient)}$$

Frequently one encounters a patient who is getting more insulin than the diet requires. This produces a minus coefficient.

Glucose utilization = 120 grams
Insulin administered = 40 units

$$\frac{120}{4} = 30 \text{ IR (insulin required)}$$

$30 - 40 =$ (minus) -10 IC (insulin coefficient)

A minus insulin coefficient suggests a number of explanations:

1. The patient may be getting insulin in too large doses which do not synchronize with the food eaten. Since insulin activity usually extends over a period of two to four hours and food digestion and absorption over from five to ten hours, excessive insulin dosage may be lost or wasted.

2. It is well known that infections interfere either with insulin production or activity.

3. Insulin injected into scar tissue may be wasted or it may leak out of the skin along the needle track.

4. The patient may be eating food in excess of that provided in the diet, thus introducing an error in the calculation.

The insulin coefficient method is a most excellent way of checking the

stealing of food which formerly was the universal sin among diabetics, and is even now occasionally practiced. Indeed, in our work we have found the insulin coefficient method of great service in detecting all kinds of errors as well as chicanery on the part of patients. By means of it we determined that a patient was not accurately measuring his insulin, his insistence to the contrary notwithstanding. We found another patient stealing insulin. This individual, a child, had purchased and secreted insulin outfits in various places and would indulge in all sorts of dietary sprees fortifying himself by the indiscriminate injection of the insulin. We have detected concealed and unsuspected infections and have used it as a clinical guide in the care of serious inflammations of various parts of the body, as bones, lungs, abscesses. In this connection it may be said that the insulin coefficient in a diabetic suffering from an inflammation is a more useful and accurate measure of the disease process than are either the leucocyte count or the temperature curve.

In the diagnosis of borderline or doubtful cases the method is particularly valuable. We have had many cases who have been under a strict diabetic regime including insulin therapy, all because traces of reducing substance were found in the urine. In some instances this reducing material was sugar, in others it was not. Many of these cases had coefficients above one hundred. They were not able to eat sufficient food to show impairment in glucose utilization. In the final diagnosis of doubtful insurance risks the method far exceeds in value and fairness the so-called glucose tolerance test, for while it is true that all diabetics give a positive reaction to this method it is not true that all who react to it have diabetes. Furthermore there is no unanimity of opinion as to the significance of the data that is afforded. Most condemning of all, it is a wholly unnatural procedure. It falsely assumes that because the body is unable to assume a sudden and very unusual load that it is not able to perform the same work if spread over a reasonable time.

In the treatment of diabetes the coefficient method is particularly valuable. The clinician has one guiding rule. He first determines how much insulin the patient can make in twenty-four hours by a careful dietary and urine study covering several days. This becomes the patient's coefficient. If this be low, insulin therapy becomes necessary. The dosage is determined by repeated tests involving the factors of time and quantity of insulin to obtain the highest degree of glucose utilization. The constant endeavor is to raise the coefficient, for by so doing, the most effective combination of diet and hormone action is secured. In these studies it may be discovered that the patient will do best with a different arrangement of diet or insulin dosage than has been employed. Sometimes three or four small doses properly spaced are much more effective than the same number of large doses. Reactions are a sure sign of wasted insulin. In this method the blood sugar becomes a guide to insulin dosage and not to total metabolism. A quantity of insulin which produces an abnormally low blood sugar two or

three hours later is partly wasted. The patient should be kept in that state of balance which will enable him to utilize to the fullest extent the insulin which he produces himself. The body weight is an important factor in the arrangement of the diet. If the patient be undernourished then the diet should be sufficiently ample to correct this factor. If he be obese it should be modified accordingly, the constant aim being to keep the patient practically urine sugar free, with a maximum insulin coefficient and the body weight properly controlled. The method permits the epicurean patient to indulge himself with safety. The pseudo-scientific food and drug fads which have grown up around diabetes can well be forgotten.

It is not claimed that the method is infallible. There are other factors than insulin involved in the diabetic process. In the metabolism of profound coma, insulin often fails to work or acts feebly. Oftentimes in the severe diabetes of childhood insulin response is not in accord with the one to four ratio, but the method, however, is just as useful a guide to helpful therapy as if it were. The insulin coefficient offers a valuable control to clinical research on diabetes, which must be done on the human. There are many unsolved problems. For the great majority of cases, however, both for diagnosis and treatment, in our hands it is by far the best method with which we have worked.

Conclusion

The problem of diagnosis in advanced diabetes is simple and presents no technical or clinical difficulties, but not so with doubtful or borderline cases. At the present time we are depending upon tests of very uncertain value, highly speculative and in a large measure illogical. If diabetes be due to a defect in the total metabolism of the individual, then tests which disclose only a slight transient or inconstant departure from the normal physiology or body chemistry and which are commonly present in other disease states, cannot be regarded as conclusive. The insulin coefficient method directly and accurately measures the capacity of the individual to utilize glucose, therefore its findings are logical and conclusive.

In like manner the criteria by which the diabetic is now dieted and treated with insulin are open to the same objections. They permit of the widest variation in therapy and are not sufficiently definite to make evident which is the best. The insulin coefficient method enables the clinician to determine with exactness the amount of insulin the patient may himself make, whether or not administered insulin is being used efficiently, and whether or not glucose is being properly utilized. Under this plan slightly elevated blood sugars and small amounts of sugar in the urine, while of interest, are of secondary importance. Its great advantage to the doctor is that he has a single guiding rule which gives him an unfailing index to the condition of the patient and for the patient, it makes it possible for him to live under the best possible conditions. For these reasons it may be regarded as the optimum method.

The Effect of the Ingestion of Burdock Root on Normal and Diabetic Individuals A Preliminary Report*

By A. A. Silver, M.D., and John C. Krantz, Jr., Ph.D., *Baltimore, Md.*

Arctium lappa or burdock is a coarse biennial weed which grows in Europe, Asia and North America. Early in the nineteenth century, it was observed that the administration of burdock root was beneficial in cases of skin eruptions, gout, rheumatism and calculous complaints.[1] For many centuries it has been utilized in the kitchen of many households and restaurants of the Japanese.[2] There the root is stripped of its bark and the pulp is sliced, boiled, seasoned, and served as a vegetable much as the occidentals serve parsnips and sweet potatoes. Coincidentally it is interesting to observe that the Japanese have a high racial immunity to diabetes.[3] Burdock has enjoyed some reputation as an alterative in constitutional blood diseases. "Burdock tea", designated as Radix Burdanae in Germany, has been regarded as an efficient blood purifier. From 1830 to 1910, burdock was recognized by the United States Pharmacopeia. Culbreth[4] lists its constituents as inulin, a bitter extract, fat, resin, levulose, and cellulose. The drug is indicated, according to this author, as a diaphoretic, diuretic, alterative, and depurative, and is useful in gout, rheumatism and in dermal eruptions.

In 1851 Bouchardat[5] observed that levulose was tolerated better by diabetics than glucose, and noted that patients with mild diabetes were aglycosuric when they ate 50 to 100 grams of this monosaccharide per day. Johanson[6] showed that levulose increased the respiratory quotient more rapidly than did glucose, and that the duration of the elevated quotient was also longer. Straus[7] recommended a daily diet of 50 to 100 grams of inulin and observed that favorable therapeutic results followed. He found also that inulin was antiketogenic and this seemed to indicate that this polysaccharide was absorbed. Tanaka[8] found inulase in the placenta and in the spleen of warm blooded animals which suggests that this polysaccharide may be split in the intestinal tract by this enzyme. The work of this investigator is substantiated by the experiments of Okey[9] who found that inulin is hydrolyzed partially by the hydrochloric acid of the stomach and that the feces of individuals fed a varied diet contains an inulin-splitting substance.

Inulin is a gamma-glucoside-fructose-ester. Krantz and Carr[10] in their

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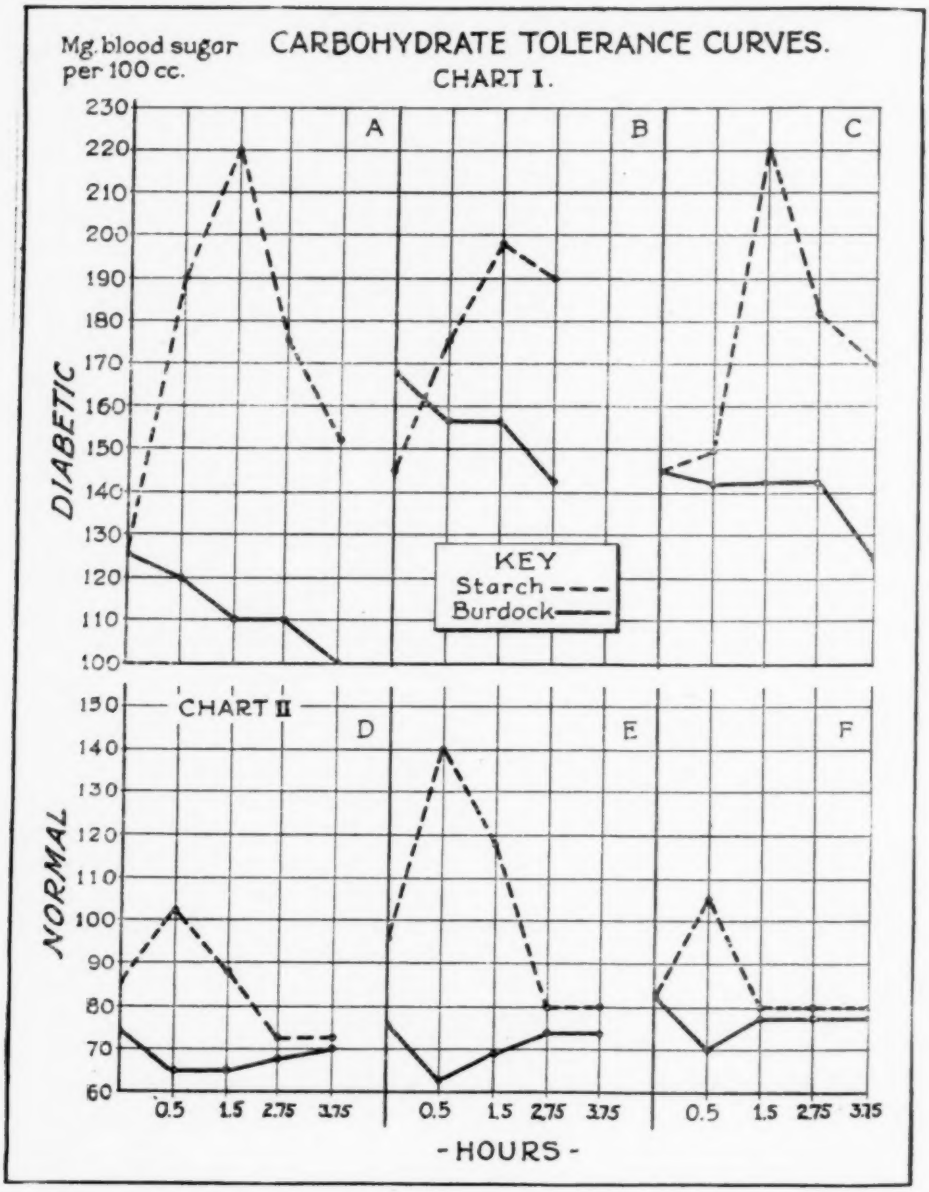
physicochemical investigations of the carbohydrate contained in *Arctium lappa,* have published evidence which seems to indicate that this substance has not the same degree of molecular complexity as inulin, as it occurs in the dahlia and in the tubers of Jerusalem artichoke. On the other hand, it corresponds to the inulenin isolated by Tanret,[11] having a molecular weight of about 1500 rather than about 5000 which is the assigned value of the molecular weight of inulin. One gram of inulin was shown by Gottschalk[12] to have a caloric value of 4.19 calories. He suggested that the usefulness of inulin in diabetes of the mild type is due to the fact that its hydrolytic product, levulose, has an insulin-enticing action. Levulose is a more labile monosaccharide than is glucose, and it may have the capacity to call forth to a greater degree than glucose, the reserve insulin of the islets of the pancreas.

Solarino[13] showed that if dogs were fed 5 grams of inulin simultaneously or shortly before or after the ingestion of 25 grams of glucose, the hyperglycemia that resulted was less than when glucose only was given. Likewise, Ciaccio[14] and Racchuisa showed that inulin lowered the hyperglycemia caused by glucose in dogs. Like Gottschalk they felt that this inhibiting action was dependent upon the action of inulin on the internal secretion of the pancreas.

Recently Root and Baker[15] and Carpenter and Root[16] observed a patient in whose diet artichokes furnished the greater portion of the carbohydrate. Although this patient remained sugar-free on this diet, the substitution on one day of an equivalent amount of carbohydrate in the form of baked potatoes was accompanied by a rise in the blood sugar and the prompt appearance of sugar in the urine. The resumption of Jerusalem artichokes on the next day was accompanied by a lowering of the blood sugar and a disappearance of urinary sugar.

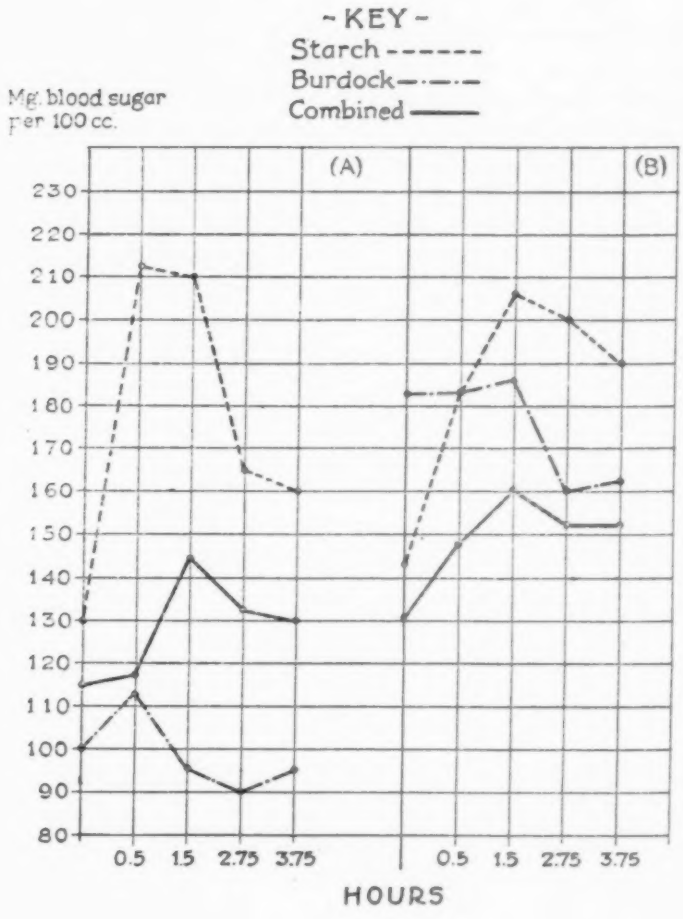
Krantz and Carr[17,18] have shown experimentally that in white rats powdered burdock root causes an increased storage of glycogen in the liver; and further that in dogs it is anti-ketogenic and has a protein-sparing action. These investigators considered these data to be evidence of the absorption and the utilization of this carbohydrate.

With the foregoing facts in mind the influence of the administration of powdered burdock root upon diabetic patients was observed. The first problem was the production of a foodstuff sufficiently palatable to be substituted easily for other carbohydrates in the diet. The dried root was powdered and extracted with ethereal solvents. This left a powder containing about fifty per cent of carbohydrate hydrolyzable into levulose, a small amount of fat and bitters. The remainder was cellulose. By exposing the powder to low heat, the fat and the bitters were driven off. Later, we found that by re-extracting the powder with an acetone-alcohol mixture, the fat and bitters were more completely removed. This left a powder containing sixty per cent of carbohydrate. A batter was made with 90 grams of the powder, 36 grams of butter, water, salt, saccharin, and a few drops of the fluidextract of ginger. Dividing this


Mg. blood sugar per 100 cc.
CARBOHYDRATE TOLERANCE CURVES.
CHART I.
DIABETIC
230
220
210
200
190
180
170
160
150
140
130
120
110
100
A
B
C
KEY
Starch
Burdock
CHART II
NORMAL
150
140
130
120
110
100
90
80
70
60
D
E
F
0.5
1.5
2.75
3.75
- HOURS -

MIXED CARBOHYDRATE
TOLERANCE CURVES

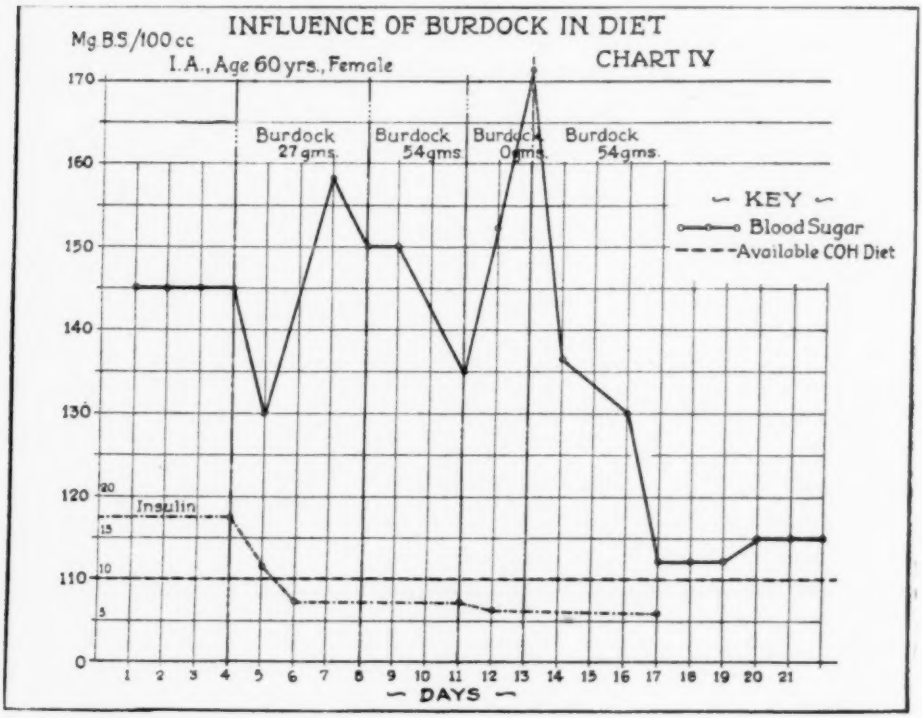
CHART III



into twelve equal parts and baking them as cookies, we obtained a cracker that contained approximately 4.5 grams of carbohydrate, 3 grams of fat, and 0.2 gram of protein.

Three non-diabetic individuals who did not have evidences of disturbance of any of the other glands of internal secretion were studied. In each instance a preliminary determination of the blood sugar was made when the patient had fasted for 12 hours, and then each one was given the equivalent of 100 grams of ordinary carbohydrates in the form of Burdock root. The preparation utilized was a powder containing 80 per cent of carbohydrate, 75 grams of which were suspended in coffee, 28 grams in a flavored gelatin and the remainder in four cookies prepared in the manner described. Determinations of the blood sugar were made one-half hour, one and one-half hours, two and three-quarters hours and three and three-quarters hours after the ingestion of the meal. As a control, on another day, instead of the preparation of burdock root the patients received 100 grams of carbohydrates in the form of oatmeal, canned corn, toasted wheat bread and banana and the blood sugar was estimated at the same intervals of time as in the original experiment. Chart No. II, graphs D, E and F, show the type of blood sugar curves obtained.

It is apparent that when the burdock diet was fed there was a preliminary decrease of blood sugar followed by a gradual rise to just below the

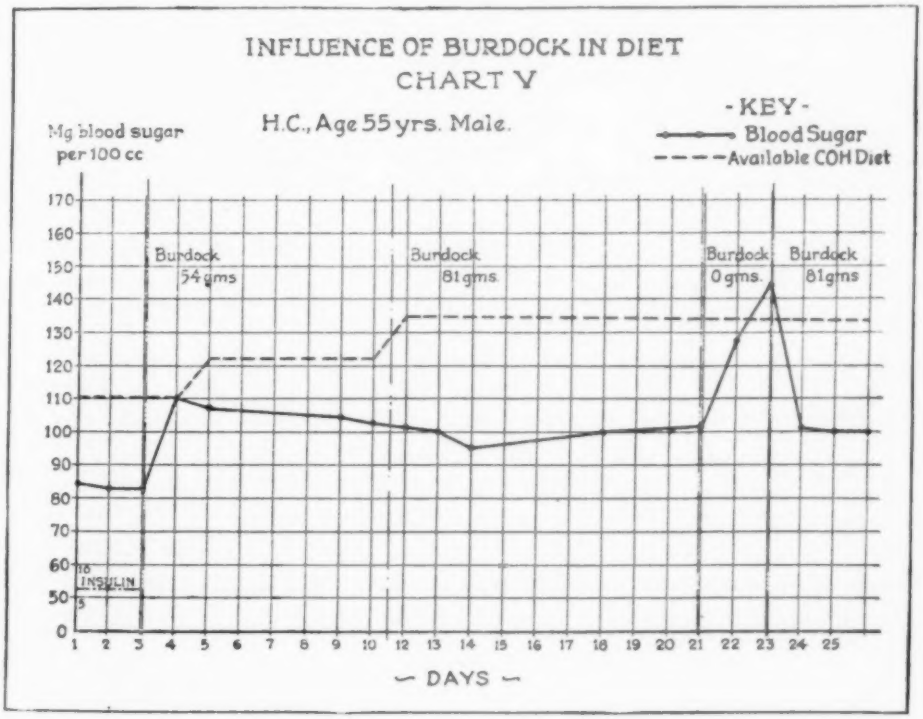


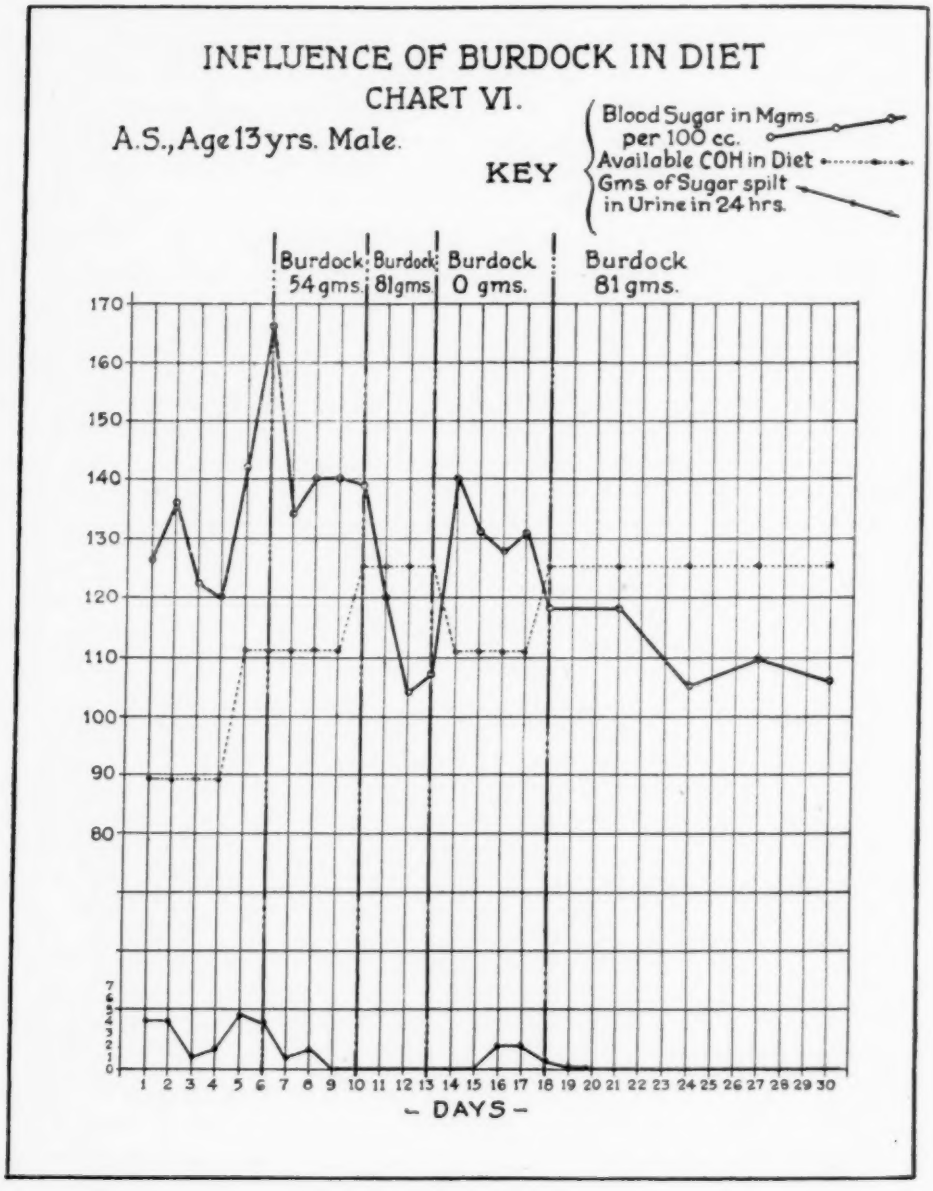
fasting level at the end of three and three-quarters hours. With the meal consisting of carbohydrates other than those in burdock, a curve similar to, but less marked than that of a normal glucose tolerance curve, was obtained.

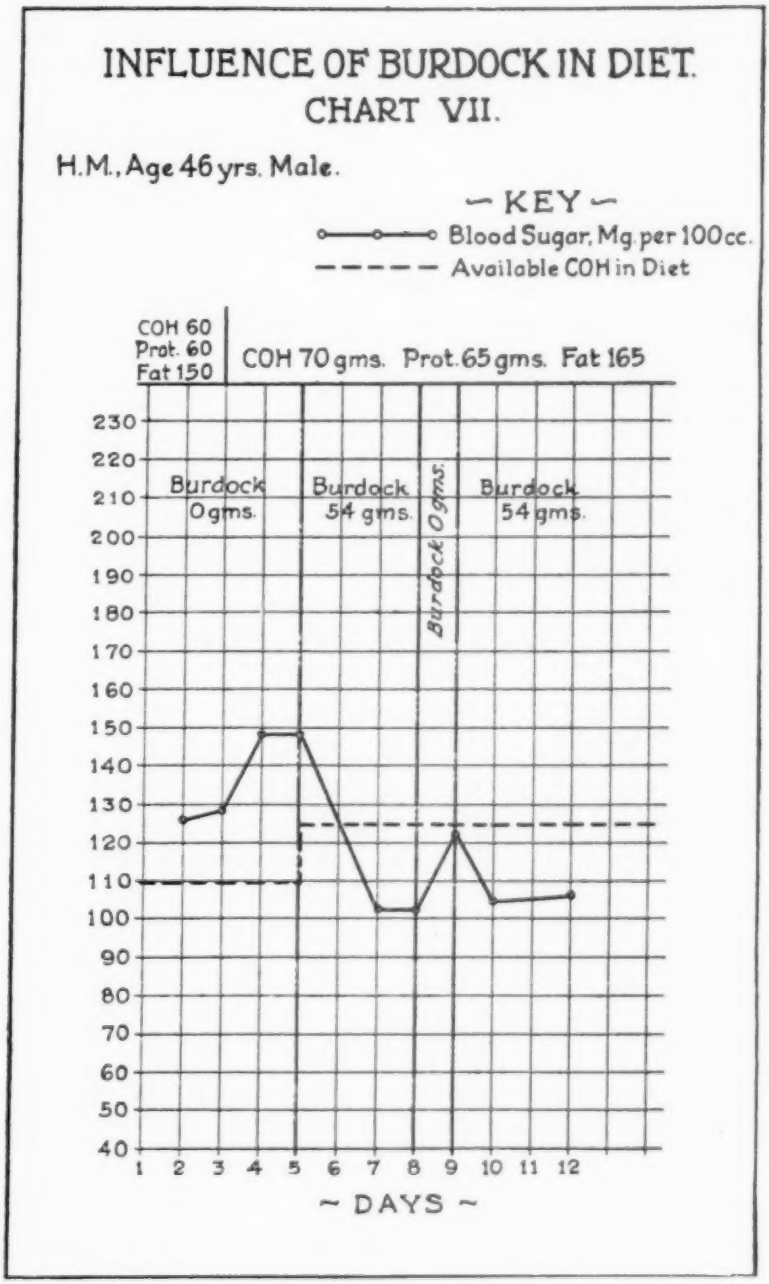
A similar experiment was carried out with known diabetic patients. To these patients we gave an amount of burdock corresponding to 33 grams of carbohydrate. On another day, under the same experimental conditions, we gave 33 grams of other polysaccharides to these patients. Similar curves were obtained with burdock; and the expected diabetic rise with slow return was obtained with the ordinary polysaccharide meal as evidenced in the following curves. (See Chart No. 1, graphs A, B and C.)

Following the thought that there was an inhibitory factor in burdock on the hyperglycemia of glucose, the following experiment was carried out. Two known diabetics were each given the burdock and non-burdock diets as above described and blood sugars taken at the same intervals. On a third day fasting-blood sugars were taken, the burdock meal was given and followed immediately by a non-burdock meal—33 grams of each. Blood sugars were again taken at the same intervals following the ingestion of the second meal. The curves obtained indicate that there is an inhibitory effect of burdock on the hyperglycemia of glucose. (See Chart No. III.)

The validity of theory of Gottschalk[12] that the ketone group of lev-

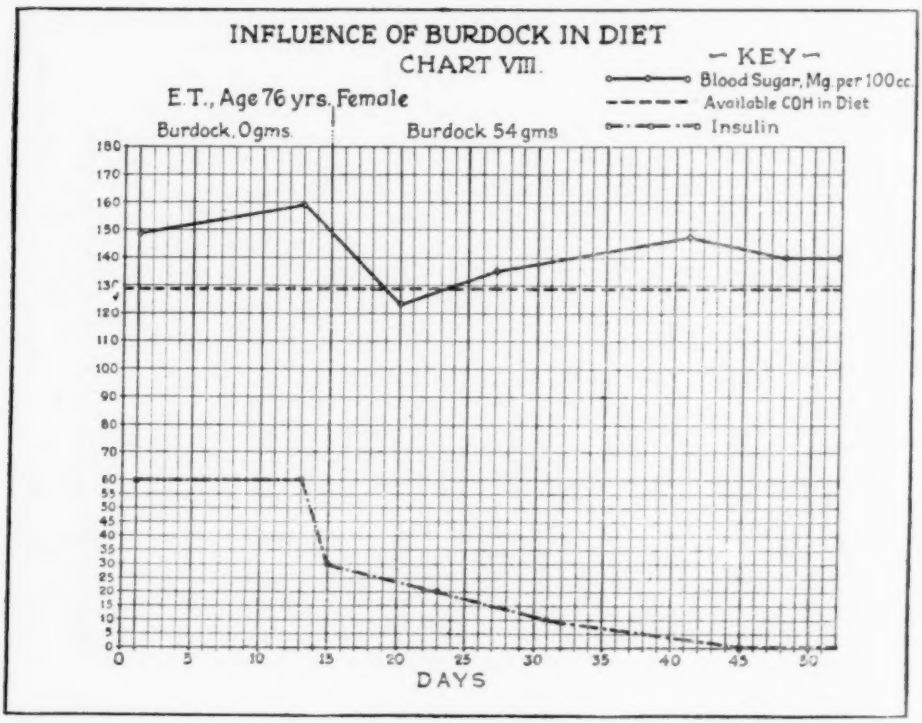


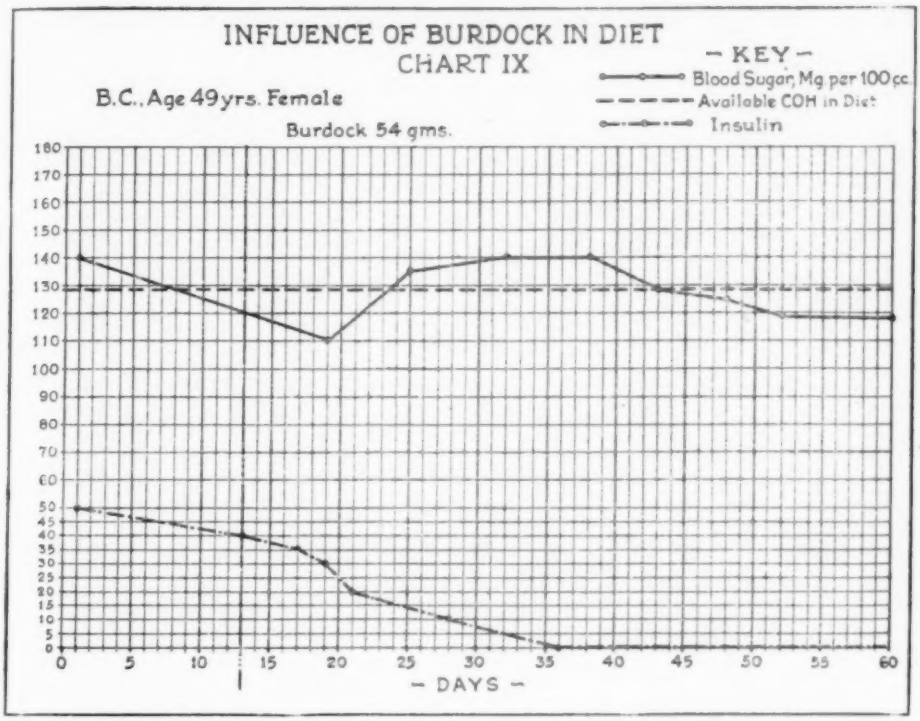

INFLUENCE OF BURDOCK IN DIET
CHART VI.
A.S., Age 13 yrs. Male.
KEY
Blood Sugar in Mgms. per 100 cc.
Available COH in Diet
Gms. of Sugar spilt in Urine in 24 hrs.
Burdock 54 gms.
Burdock 81 gms.
Burdock 0 gms.
Burdock 81 gms.
170
160
150
140
130
120
110
100
90
80
7
6
5
4
3
2
1
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
– DAYS –


INFLUENCE OF BURDOCK IN DIET.
CHART VII.
H.M., Age 46 yrs. Male.
~ KEY ~
Blood Sugar, Mg. per 100 cc.
Available COH in Diet
COH 60 Prot. 60 Fat 150
COH 70 gms. Prot. 65 gms. Fat 165
Burdock 0 gms.
Burdock 54 gms.
Burdock 0 gms.
Burdock 54 gms.
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
1 2 3 4 5 6 7 8 9 10 11 12
~ DAYS ~

ulose is capable of calling forth to a greater degree than glucose, the reserve insulin of the islets, seems to be substantiated by the foregoing results. On the other hand, however, the presence of levulose may hasten the polymerization of the blood glucose into glycogen and in this manner lower the blood sugar level.

Following this work, we began the use of burdock root in the form of crackers as above described as a substitution for the carbohydrates in the diets of several diabetic patients. In accompanying charts IV, V, VI, VII, VIII and IX we have plotted the course of several diabetic patients receiving burdock therapy. In these cases the dosage of insulin was decreased as burdock was administered. When the blood sugar approached normal the burdock was replaced by other polysaccharides. Immediately there was a marked rise in the blood sugar which returned at once to its former level on replacing the burdock in the diet. This we found to happen in each instance where the foregoing procedure was carried out. In all cases while burdock was being administered there was no glucosuria. However, upon removing the burdock from the diet of diabetic patients and replacing it by other polysaccharides (Uneeda biscuits) glucose appeared in the urine. Stool examinations on patients receiving burdock for three successive days showed no copper-reagent-reducing substances after hydrolysis with dilute hydrochloric acid.





Summary

1. The carbohydrate in burdock root was absorbed and utilized by certain patients with diabetes mellitus.
2. In the cases reported burdock root seems to exhibit an inhibitory action on the hyperglycemia caused by the common polysaccharides.
3. Powdered burdock root may be easily administered to patients in the form of palatable crackers.
4. Mild diabetic patients may be kept at normal blood sugar levels and aglucosuric by the administration in their diets of crackers made from powdered burdock root.

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Diabetes in the Negro Race*†

By Eugene J. Leopold, M.D., *Baltimore, Md.*

It was not so many years ago that diabetes mellitus was considered a rare disease in the colored race. In fact, it is rather common today to hear usually well informed physicians express this belief. This is not altogether surprising since the literature on the subject is indeed meager. It is hoped that such facts as I am able to present will stimulate further study of the subject.

Osler's "Principles and Practice of Medicine" until about ten years ago said diabetes mellitus was rare among negroes. I. I. Lemann of New Orleans was the first to call to our attention statistics which disproved this statement. In 1911[1] he published studies based upon 61,298 admissions to the Charity Hospital which showed that negroes furnished 40 per cent of the admissions to the hospital and 30 per cent of the diabetic admissions.

The incidence rate was .047 per cent against a white rate of 0.072 per cent. In later studies[2] based on 148,671 admissions during the years 1921-1927 the incidence rates had risen and were 0.34 per cent for negroes as compared with 0.23 per cent for white admissions—higher for the negroes than for the white.

More recently Bowcock reported from Atlanta, Georgia, on the experience of the Grady Hospital and the Gray Clinic with diabetes mellitus in the negro. He[3] found among 26,858 admissions to the colored hospital between 1921 and 1928, 112 patients with diabetes, giving an incidence of 0.42 per cent of the admissions.

Table I gives some facts concerning diabetic deaths in Baltimore[4] for the years 1928 to 1930 inclusive. It shows that negroes formed about 18 per cent of the population of the city and had a considerably higher death rate per hundred thousand inhabitants as compared to the white population, 20.8 and 13.2 respectively. Considering the deaths from diabetes, we find 18 per cent of the population showing a rate of 18.31 diabetic deaths per hundred thousand inhabitants. The remaining 82 per cent white population had a rate of 28.66 per hundred thousand inhabtants. Roughly, for every ten deaths of diabetes per hundred thousand inhabitants among whites, 6.4 negroes died of the disease. One can therefore, no longer consider the disease as a rarity among the negroes of Baltimore. From another viewpoint the same fact becomes evident; during the past three years, ending January 1, 1931, 646 new cases of diabetes mel-

*From the Johns Hopkins Hospital Out Patient Department Diabetic Clinic.

†Presented before The American College of Physicians, Section E, Baltimore, Maryland, March 26, 1931.

TABLE I

Year	Population			Deaths from All Causes			Rate per 100,000 Inhab.		
	Total	White	Negro	Total	White	Negro	Total	White	Negro
1928	792,744	655,827	136,917	11,929	8,965	2,964	15.1	13.7	21.6
1929	799,675	659,438	140,237	11,629	8,747	2,882	14.6	13.3	20.7
1930	806,607	663,050	143,557	11,238	8,422	2,816	13.9	12.7	19.6
Aver.	799,675	659,771	140,237	11,578	8,711	2,220	14.4	13.2	20.8

Year	Diabetic Deaths						Diabetic Deaths in Total Deaths, Per Cent		
	Number			Rate per 100,000 Inhabitants					
	Total	White	Negro	Total	White	Negro	Total	White	Negro
1928	229	202	27	28.88	30.81	19.72	1.92	2.25	0.91
1929	109	166	23	23.63	25.17	16.41	1.62	1.90	0.80
1930	226	199	27	28.02	30.01	18.81	2.01	2.36	0.96
Aver.	214	189	25	26.84	28.66	18.31	1.85	2.21	0.89

1930—Population	82%	White	18%	Negro
All Deaths	75%	White	25%	Negro
Diabetic Deaths	76%	White	24%	Negro
Diabetic Deaths	2.36%	White	0.96%	Negro

TABLE II

Year	New Admissions to Dispensary				Diabetic Admissions									
	Male		Female		Male		Female		Total		Incidence Per Cent			
	White	Negro	White	Negro	W	N	W	N	W	N	W	N	Lemann	Bowcock
1927-28	6,346	2,732	6,081	3,701	56	16	110	42	166	58	1.33	0.90		
1928-29	5,219	2,056	4,638	2,749	60	14	92	51	152	65	1.54	1.35		
1929-30	4,653	1,940	4,562	2,776	48	18	91	48	139	66	1.51	1.45		
Totals	16,218	6,728	15,301	8,226	164	48	293	141	457	189	1.45*	1.27*	3.4	4.2

Total White, 31,519 Total Negro, 14,954
1.45% of white are diabetic.
1.27% of negro are diabetic.
*May be low as compared to the figures of Lemann and Bowcock because of limited intake of negro patients.

litus were admitted to the Diabetic Clinic of the Out Patient Department of Johns Hopkins Hospital. Table II shows that of 46,473 new admissions to the Out Patient Department 14,954 were negro patients, 31.9 per cent of the admissions. Among the 646 new cases of the Diabetic Dispensary, 189 or 28.8 per cent were negroes. These figures are somewhat lower than those given by Lemann, 40 per cent admissions and 30 per cent diabetic, and may be due to smaller proportion of negro population in Baltimore as compared to New Orleans. A study made in 1922 of 252 active cases in our clinic showed negroes to represent 22 per cent of the clinic attendance. The average white and colored incidence for the three years was 1.45 per cent and 1.27 per cent respectively. Considering individual years, white incidence was 1.33 per cent, 1.54 per cent and 1.51 per cent and colored was 0.90 per cent, 1.35 per cent and 1.45 per cent. The close approximation of the colored to white incidence may mean that the negroes have a special liking for our clinic. It is out of line with the white and negro death rates given above which show that about 60 per cent as many negroes died as did white persons per hundred thousand inhabitants. Yet it, too, points to the fact that diabetes is a rather common disease among the negroes of Baltimore.

Diabetic deaths in Baltimore in the last three years show a great preponderance of the disease among females. Table III indicates that averaging the three years, 69.2 per cent of the diabetic deaths were in females. When

TABLE III
Diabetic Deaths in Baltimore

Year	Total Deaths		Per Cent Female	Males		Per Cent Negro	Female		Per Cent Negro	Per Cent of Female Deaths	
	Male	Female		White	Negro		White	Negro		White	Negro
1927	63	133	67.8	57	6	1.06	114	19	17.7	57.2	76.0
1928	78	151	65.5	71	7	0.99	131	20	16.0	57.2	73.6
1929	54	170	75.9	50	4	0.80	116	19	10.2	54.0	80.0
Aver.			69.2							56.1	76.5

we differentiate between the white and negro deaths, we find the former comprise 56.1 per cent of all diabetic deaths and the latter 76.5 per cent.

In our series of cases in the Clinic 66.2 per cent were female, 64.1 per cent white females and 74.1 per cent colored females.

The percentage of white female deaths, 54.0 to 57.2, agrees closely with Joslin's division of clinical diabetics, 55 per cent female and 45 per cent male in the middle decades of life. It is evident both from the death statistics of Baltimore and from the figures from our clinic that diabetes is more common among colored females than it is among white females.

A study has been made of 100 unselected negro cases which were treated at the Clinic during the past year. In this group we find 71 per cent are females and 29 per cent males. All of the sources show that diabetes mellitus is found among negroes in a ratio of 30 to 35 per cent male and 65 to 70 per cent female. These figures are somewhat different from most of the reports on the subject. The earlier reports analyzing the occurrence of diabetes by sex were from foreign clinics and showed a preponderance of male diabetics as high as 77 per cent.[5] Joslin found in a study of 2,646 cases occurring between 1922 and 1927, a reversal of this male preponderance and noted that 55 per cent were female and 45 per cent male. It would seem that negro females are especially prone to the development of diabetes. Bowcock has pointed out that the usual diet among negroes is especially rich in caloric values, in-

cluding such food stuffs as pork, cornbread, fat meats, and potatoes. The tendency of the negro to live on these food stuffs produces obesity and to this the elderly female is especially prone. Joslin has pointed out that diabetes has increased in frequency even more rapidly among the older negro females than it has developed among white females of the same age group. This seems to be true in the group we have analyzed.

The study of our 100 cases by the age at which they first came under observation is shown in Table IV.

the time of the first visit to the clinic. Perhaps also the well known uncertainty of the negro as to his age may be a factor. Naturally diabetes has in the majority of instances been in existence for some years previous to the first visit. In justification of our classification, let me call attention to the lack of attention given by the negro to symptoms of the disease and the difficulty experienced frequently in attempting to obtain precise facts for the history.

A patient with a weight of ten pounds in excess of the ideal for sex,

TABLE IV
Age Distribution by Decades of 100 Diabetics

Decade	I	II	III	IV	V	VI	VII	VIII
Male	0	2	2	8	6	7	3	1
Female	0	1	2	8	32	28	4	2
Total	0	3	4	16	32	35	7	3
Per cent of 100 cases	0	3.0	4.0	16.0	32.0	35.0	7.0	3.0
Joslin 1927—White	4.6	7.0	8.8	13.0	24.0	26.3	12.8	2.6
Lemann 1928—Negro	—	—	15.5	26.8	31.0	19.7	—	—

Sixty-seven per cent of our group are found in the fifth and sixth decades as compared with 50.3 per cent in white patients as found by Joslin in 1927, and 50.7 per cent in negro patients found by Lemann in 1928. Since children up to the age of twelve years are treated in the Harriet Lane Home, we have no patients in the clinic under thirteen years of age. We have a smaller percentage of cases in the second and third decades than reported by Joslin and in the third and fourth decades than reported by Lemann. Perhaps this difference may be due to the fact that we have classed our cases according to their ages at

age, and height we have considered as obese. It may not be entirely fair to use white standards of weight for the colored race, but we know of no standards for the negro. On this basis 67 per cent of all the cases were obese, 67.6 per cent of the seventy-one females and 67.0 per cent of all the cases. Bowcock found 92 per cent of the females in his series were obese. Perhaps the negro of the more northern districts shows less obesity than in the South because his dietary habits have been modified. Yet this is not borne out. For in the age group from 40 to 60 years, obesity was present in 86.4 per cent of the cases.

Joslin has emphasized the importance of obesity as a factor in diabetes.[6] In a recent study of 1,000 cases he found 77 per cent were above normal weight. It would seem that the middle-aged female negress is even more prone to fatness than is the white of the same period. Besides, as Bowcock pointed out, instances of excessive overweight are far more common among the negresses than among the white females.

Again, basing our statements upon the date of the first visit to the clinic, there are in this group of 100 cases, 19 cases known to the clinic for five years or longer. The longest known is a female who came to the clinic in 1917, aged 52 years, and was placed on insulin in 1924. There is also a male, aged 41 years when he came to the clinic in 1918, who has done well on diet alone. In the group of 19 there are 14 females and 5 males. Two were in the fourth decade at the first visit, 6 in the fifth, and 11 were 50 years of age or older. Lemann found the longest duration among those of his cases in whom onset was in the fifth decade. Insulin is being taken by seven of our cases, two males and five females.

It is a well known fact that syphilis is very common among negroes. Lemann found[7] among 68,004 negroes in New Orleans evidence of acquired syphilis in 56 per cent of the cases. In our series every case has had the Wassermann test, both by water-bath and ice box methods. Twenty (20 per cent) of these tests were positive and one test was doubtful. This case was a male who gave a history of having had syphilis some years before. He had taken a series of treatments before he came to the clinic. Eight other males were positive and fifteen females. The amount of syphilis seen in our clinic is in agreement with the findings of Paullin, Davidson and Wood[8] among negro patients in Atlanta, 22 per cent among Outpatient Department cases and 20 per cent of the negro hospital admissions.

Warthin and Wilson[9] have emphasized the importance of syphilis as a cause of diabetes mellitus. We cannot agree with these authors since practically all of our syphilitic cases have had intensive antisyphilic treatment cojointly with their diabetic therapy.* In no instance have we been able to note any improvement of the diabetes which could not be the result of controlling their hyperglycemia by diet alone or diet and insulin. We have had several cases in which blood and spinal Wassermann tests have become negative under treatment without showing any effect upon the diabetic conditions. In fact, the latter has progressed as a result of inability to keep diet.

Based on clinical observation with only infrequent eye examinations, 54 of the 100 cases gave evidence of hardening of the peripheral arteries beyond that to which they were entitled by age. Bowcock noted this complication in 55 per cent of his cases. Joslin, with more exact examinations, has found an average of all ages of 80 to 90 per cent.

We have found a systolic blood

*[Note by Editor: Antisyphilitic treatment cannot be expected to remove fibrosis or sclerosis already established, or to restore island tissue.]

pressure of more than 150 mm. in 38 cases in which reading has been noted. This is 40.5 per cent of the cases. This is in rather close agreement with the findings of Bowcock.

The occurrence of gangrene in our series is surprisingly small. It is true that we have adopted for use in the clinic a card of directions for the care of the feet as suggested by Joslin. This does not, however, seem to be a factor in the infrequency with which we have met this serious complication in this series. Three of the four cases of gangrene showed the condition when they came to the clinic. The cases were equally divided between males and females, two each. Three of these resulted in mid-thigh amputation. The fourth suffered the loss of a big toe. Lemann noted the condition in 15 per cent of his hospital admissions which might be due to the fact that this serious complication practically always necessitates hospitalization. Another factor explaining the lower incidence is that the negroes of Baltimore are perhaps on a higher sanitary and hygienic level than those of New Orleans, and do not expose their feet as commonly to the elements which Lemann thinks helps to explain the high incidence of gangrene in his cases.

The ferric chloride test of the urine was positive in 14 per cent of our series, 10 females and 4 males. Four cases were admitted to the hospital in coma and all were rescued by insulin treatment. Lemann had 15 per cent of coma in his series.

Fifteen patients, 15 per cent, showed changes in the optic lens. There were twelve females and three males. Our youngest case was 26 years old when a cataract was noted in his left eye and, upon his return recently, after being absent from observation for seven years another was found in his other eye. Joslin has noted cataract in about 10 per cent of his cases. Spalding and Curtis[10] found it present in 13 per cent of their cases. Since the opening of the Wilmer Ophthalmological Clinic three years ago we are seeing more cataracts constantly. We had one case of bilateral glaucoma and numerous instances of retinitis and other eye conditions.

Thirty of our 100 cases have had insulin treatment, 22 females and 8 males. Lemann gave 19 of his cases insulin and Bowcock likewise. Joslin has stated recently that two-thirds of his cases are now using insulin. The smaller percentage in our series is due to several factors. We have maintained that no clinic case should have insulin unless it actually needs it. Our usual diets have contained from 60 to 80 grams carbohydrate until recently when we have increased this to 100 grams. Cost is an important factor in a group such as we have under consideration. But it does not seem that the negro has any difficulty in carrying out the systematic insulin treatment when it is necessary. It is surprising how few infections we have seen among negroes who are giving themselves the injections. In many instances they are examples of the most complete co-operation despite a meagerness of learning and lack of education. It has not been unusual in the clinic to find a negro who cannot read or write using insulin over years and keeping diet as carefully as do some

of our model white patients. Just one example is case 52, a female, aged 52, known to us since 1917, adjusted to insulin in 1924. She has taken her insulin constantly since then and has effected a 40 per cent reduction in dosage. She has never shown sugar since 1924.

All of these cases were adjusted to insulin in the hospital. We do not attempt to start a patient on insulin in the Clinic, but always give them a period of hospital study before starting injections.

Since this study is one of active cases seen during the past year, we have no deaths to report.

Economic problems occur more frequently among negro patients of an Out Patient Department than among the white cases. These are, in many cases, surmounted by efficient Social Service work. These problems concern the actual providing of diet and, when necessary, of insulin. Perhaps the greatest hindrance among the females is in their occupation as cooks. While the best of colored, as of white, cooks need not taste their cooking to be sure of its proper preparation, many cooks are not so good and must sample the food they prepare.

Summary

1. Diabetes mellitus is not an uncommon disease among negroes.
2. The death rate of diabetes mellitus in Baltimore in 1930 was 28.02 for white persons and 30.01 for negroes per hundred thousand inhabitants. White deaths from diabetes were 2.36 per cent of all deaths and negro deaths were 0.96 per cent.
3. Among the new admissions to the Out Patient Department of Johns Hopkins Hospital negroes formed 31.9 per cent, and 28.8 per cent of the new admissions to the Diabetic Clinic.
4. Diabetes in the negro is even more common among females than in the white race.
5. A study of 100 cases of diabetes in the negro reveals:
   - Sex: females were about three and one-half times as common as males.
   - Age: 67 per cent of the cases were between the ages 40 and 59 years.
   - Obesity: played the major factor in etiology; 86 per cent of the older females were obese.
   - Duration: in 19 per cent of the group, the patients had been known to the clinic more than five years.
   - Syphilis: does not play an etiological factor in the cause or progress of diabetes.
   - Arteriosclerosis and hypertension: were about as common as in non-diabetics of the same age.
   - Gangrene: was seen only four times in the 100 cases.
   - Acidosis: occurred in 14 per cent of the cases.
   - Cataracts: occurred in 15 per cent of the cases.
   - Insulin: was used in 30 per cent of the cases.
6. Diabetes in negroes is not different in any way from the disease as found among white people.

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Syphilitic Aortitis in Retrospect*†

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THE bedside-necropsy correlation of disease was in a considerable measure responsible for the dawn of modern clinical medicine in the late eighteenth and the early nineteenth centuries. In a majority of instances such studies can admittedly reveal only the irretrievable end products of disease; yet from such determinations it has not infrequently been possible to explain the clinical manifestations of a given entity and to discern its consecutive steps to the fatal termination. In more recent years other allied sciences have lent their impetus to the advance of clinical medicine; but the clinico-pathologic orientation still constitutes one of the most fruitful sources of the maintained growth in medicine.

Visceral syphilis has afforded an ideal field for such correlated studies, and in this direction syphilitic aortitis has received particular attention from Scott,[1,2,3,4,5] Saphir,[3,4] Martland[6] and others. In the conviction that further profit must be forthcoming from similar studies, the records of the Wisconsin General Hospital have been reviewed over a period of four years. During this time twenty-one patients have succumbed to syphilitic aortitis. Since the pathologic diagnosis has served as the ultimate criterion for the inclusion of each case in the present series, the accustomed order of affairs has been reversed and the pathologic background will be considered before the clinical analysis.

Accordingly the pertinent gross cardio-vascular findings in a typical subject (case 18) are abstracted from the report of the Department of Pathology, University of Wisconsin:

The cardiac apex lies under the seventh rib, 13 cm. to the left of the midline. In situ the heart is twice as large as the subject's clenched fist. The pericardium is smooth but slightly edematous. The pericardial cavity contains 100 cc. of clear yellowish-brown fluid. The heart weighs 623 grams. The right heart is dilated. The apex is made up of the hypertrophied left ventricle. There is a soldier's patch over the anterior aspect of the right ventricle. The several valvular rings measure as follows: tricuspid 14 cm., pulmonic 8 cm., mitral 12 cm. and aortic 10 cm. The left ventricle averages 14 mm. in thickness and the right ventricle, 9 mm. The aortic arch ranges from 7.5 to 8 cm. in circumference. The friability of the myocardium is decreased and it sections with increased resistance. The hydrostatic test proves the aortic valve to be incompetent. The aortic cusps show marked thickening at their bases with calcification. The commissures are widened. The coronary orifices show definite partial occlusion; but the several branches of the two coronary arteries show only occasional small atheromatous plaques.

The thoracic aorta shows a saccular dilatation involving the last portion of the de-

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scending arch. Where the dilated arch impinges upon the vertebral column, there has occurred erosion of the body of the sixth thoracic vertebra on its lateral aspect. The entire thoracic aorta is dilated and on section presents many atheromatous plaques, with overlying ulceration in some instances. The aneurysmal sac is occupied by a dense laminated organized thrombus, which has somewhat shrunken from the wall of the same on one side and on the other aspect presents a smooth surface medially or to what was the restored blood channel. Below the diaphragm the atheromatous changes in the aorta are distinctly less marked.

Dr. C. H. Bunting has kindly supplied the histologic description of the heart and the aorta:

The myocardium shows hypertrophy with arteriosclerotic changes in the coronary branches. There are diffuse patchy areas of myocardial degeneration, which consist of well vascularized, recently organized infarcts of microscopic dimensions. Occasionally there are found small cellular masses composed of a few epitheloid and lymphoid cells without characteristic arrangement, but which might be interpreted as degenerated gummata.

The sections of the aorta show marked lymphoid infiltration with a few plasma cells about the vasa vasorum in the adventitia and media. The intima shows marked fibrous thickening and lymphoid infiltration. While these sections of the aorta and others taken through the sinus of Valsalva show unmistakable evidences of syphilis, no gummata can be demonstrated.

Turning to the clinical record the following essential notes are gleaned:

The subject of this necropsy was an adult, white male 40 years of age who had been a moulder by occupation. His chief complaint on admission to the hospital had been shortness of breath, which had been remarked seven weeks previously, coincident with an acute upper respiratory infection. A cough which had appeared at the onset had been definitely aggravated by exertion and over-heating. A week after the onset a sore aching feeling had appeared in the precordium and this sensation had persisted up to the time of admission, as had the dyspnea. In addition there had occurred a pain in the left side of the back about a year before the onset of the present trouble. This pain had grown so severe that at the time of entrance the patient could not lie on the left side. Sleeplessness had ensued and added to this the periodic experience of a sudden awakening at night with a profound inability to get his breath had been noted. A sense of suffocation with a struggle to get air had been the patient's analysis of these episodes.

The inventory by systems had failed to elaborate the above story and the past medical history had revealed no illness of significance. The patient had denied the occurrence of venereal disease in any form.

The social history had been deemed especially important in the occupational and marital details. Born in Poland, the patient had come to America at 21 years of age. His work had always been laborious as a farm hand and as a moulder. Married first at the age of 27, his first wife had died one year later of an acute abdominal condition, the nature of which had been unknown to the patient. There had been no issue from this marriage. Three years later he had married a second time. This wife remains living and well. Three children by this wife are living and well; a fourth had died in infancy of unknown cause.

The family history is irrelevant.

The pertinent physical findings had been largely circulatory and are herein briefed: Orthopnea and cyanosis had been noted. The apical impulse had been noted in the left sixth interspace 12.5 cm. from the midline. Further systolic impulses had been observed in the second and third interspaces. A double thrill had been palpated over the second interspaces close to the sternum to either side. A supracardiac cap of dullness had been demonstrated. The cardiac borders had been noted thus:

Right	*Interspace*	*Left*
mm.		mm.
42	2	31
48	3	44
46	4	95
	5	126
	6	148

A loud blowing systolic and a diminuendo diastolic murmer had been audible over the entire precordium. A separate apical systolic murmur had been noted. The transmission as well as the point of maximum intensity of the several murmurs had been rendered difficult of elicitation by reason of their loudness and wide dispersion. The peripheral pulse had been ill-sustained and a well marked Duroziez's sign had been established in the femoral arteries. There had been a pronounced capillary pulse. The blood pressure had registered 160 mm. of mercury systolic and 58 mm. diastolic. The venous pressure had been 10 cm. of water. The other signs of note had been the showers of basal congestive râles and the enlarged liver, palpable 10 cm. below the costal margin.

The clinical impression had been syphilitic aortitis with aneurysm of the arch, aortic insufficiency, cardiac hypertrophy and dilatation with relative mitral insufficiency, to which had been added the evidences of decompensation in chronic passive congestion of the lungs and liver.

The laboratory findings bearing directly upon the diagnosis had been:

a—Blood Wassermann reaction ++++.

b—Electrocardiogram showing left ventricular predominance, negative T_1 and slurred R_2.

c—Roentgenologic studies repeatedly demonstrating enormous widening of the cardiac shadow particularly in the left ventricular region, increase in the aortic width with sacculation in the descending arch and erosion of the body of the sixth thoracic vertebra.

The clinical course during the hospital stay had been marked by persistence of nocturnal pain. At times such attacks had been initiated by a substernal pain oppressive in nature and persistent. Occasionally a choking spell had occurred and had been accompanied by great numbers of inspiratory and expiratory wheezes and squeaks throughout the chest. Later dysphagia had become apparent. A positive centrifugal venous pulse had been noted shortly after admission and had favored the conclusion of a tricuspid insufficiency. Several syncopal attacks had marked the further progression of this course. As a rule bloody frothy expectoration and obvious pulmonary edema had attended such attacks. Throughout the period of hospital observation the backache had constituted the one constant complaint. As a rule there had been no exact localization to the same; but it had always been left-sided and had radiated about the lower left chest, although to a lesser degree there might have occurred some radiation to the right at times. Death had resulted on the seventieth day from progressive circulatory failure.

Accordingly it would appear that every detail of the pathologic picture had been anticipated in this instance by the clinical findings and diagnosis. The nocturnal dyspnea, posterior root pains, dysphagia, and the physical and roentgenologic findings of an aortic dilatation and regurgitation with cardiac enlargement occurring in a man of 40 years could leave little doubt as to the etiologic background. The sequence of events was equally apparent. The positive Wassermann reaction was merely confirmatory. The marital history, as is so frequently the case, gave no directional information. Exception may well be taken to the choice of so full blown a case of syphilitic aortitis as a type; and it is further admitted that the division as utilized by Willius,[7] syphilitic aortitis, syphilitic aortitis with aortic insufficiency and thoracic aneurysm has obvious advantages. None the less the cases herein considered represent end products and as such the above instance is a distinctive example.

The pathologic and the clinical findings for the entire group (21 cases) have been digested in Table I.

The heart's weight constitutes the first point of pathologic comparison. It was recorded in 17 instances, the re-

TABLE I

SUMMARY OF THE PATHOLOGIC AND THE CLINICAL FINDINGS.

No.	HEART				Age	Sex	Occupation	Marital History	CLINICAL COURSE				Associated Syphilis	Death
	Wt. (gms.)	Aortic Ring	Coronary Sclerosis	Myocardial Degenerat.					Symptoms	Diagnosis: Clin.	Diagnosis: Wass.	Diagnosis: X-ray		
1	250	6.5 cm.	None	None	31	M	Laborer	Single	Mental status precluded determination.	0	++++B ++++SF	—	General paresis	Bronchopneumonia complicating malarial therapy.
2	371	8 cm.	Slight arteriosclerosis	Fibrous	52	M	Laborer	Married 8 yrs. 2 children; 2 miscarriages	Initial lesion 12 years ago.	+	O-B ++++SF	+	Tabo-paresis	Paralytic ileus after malarial therapy.
3	670	8 cm. dilatation beyond ring.	Patent; atherosclerosis	Pale; fibrous	53	M	Automechanic	Married — 6 children; 3 miscarriages	Progressive dyspnoea, 4 yrs.; nocturnal paroxysms for 6 months; precordial oppression.	+ Aneurysm	++++B	+	0	Circulatory; pulmonary thrombosis with infarction
4	—	8 cm. somewhat dilated.	Little atherosclerosis	Few gray patches	57	M	Upholsterer.	Single	Entirely neurologic	+	++++B ++++SF	+	Encephalomyelitis; chorioretinitis; optic atrophy.	Cerebral hemorrhage.
5	458	7.5 cm. dilatation distally; calcification at base	Atheromatous plaques & calcification.	Gray patches.	58	M	Tailor	Married 31 yrs. No pregnancies.	Asthmatic paroxysms for 8 yrs.; later nocturnal dyspnoea; general anasarca	+ Aneurysm	O-B O-SF	+	0	Progressive circulatory failure
6	677	7.5 cm.	—	—	50	M	Laborer	Married 15 yrs. 1 miscarriage	Dyspnoea for 1 year; hemoptysis; edema of feet & legs; recent orthopnoea; precordial oppression.	+	O-B	+	0	Sudden pulmonary edema after progressive failure.
7	383	7 cm.; scarring & puckering at base.	Narrowing and extreme sclerosis	Fibrosis	45	M	Clerk	Married 7 yrs. No pregnancies	Initial lesion 13 yrs. ago Dyspnoea 10 days— paroxysmal nocturnal; precordial pain referred to left arm, relieved by nitrites.	+	+ B ++++SF	—	Meningovascular lues.	Sudden death
8	350	7.5 cm.; few warty vegetations.	Patent; atherosclerosis	Fibrosis	54	M	Clerk	Single	Psychotic	0	++++B ++++SF	+	Tabo-paresis	Melanosarcoma

TABLE I—(Continued)

No.	HEART				Age	Sex	Occupation	Marital History	CLINICAL COURSE				Associated Syphilis	Death
	Wt. (gms.)	Aortic Ring	Coronary Sclerosis	Myocardial Degenerat.					Symptoms	Diagnosis Clin.	Wass.	X-ray		
9	400	7 cm.; puckered, adherent; multiple dilatations above.	Slight atherosclerosis	0	55	M	Laborer	Widower; wife died 4 yrs. ago Tuberculosis No pregnancies	Cough for two months; hemoptysis daily; increasing hoarseness; aching left shoulder.	+ Aneurysm	O-B O-SF	+	0	Hemorrhage from rupture of aneurysm into left upper lobe
10	465	9 cm.; leaflets thickened slightly	None	Fibrous; some necrosis	52	F	Housewife (Laborious work)	Widow 17 yrs. 4 children; no miscarriages.	Dyspnoea to orthopnoea 3 years; choking sensation; substernal oppression; hemoptysis.	+	++++B	+	Tabes	Progressive circulatory failure.
11	443	7.5 cm.; cusps hardened and sclerotic; vegetations.	Single plaque	Atrophy of fibres	46	F	Housewife	Married 16 yrs. 6 children; 1 miscarriage (late).	Early fatigue and dyspnoea for 3 years; cough and palpitation.	+	++++B	—	0	Circulatory failure of vegetative endocarditis
12	280	8.5 cm.; fusion of cusps; calcified base.	Patent atherosclerosis	Soft grayish patches of fibrosis	65	M	Machinist	Married 46 yrs. 2 children; then two miscarriages.	Gastric crises for ten years.	+	O-B O-SF	—	Tabes	Cerebral deterioration; bronchopneumonia
13	290	8 cm. Few vegetations.	Atheromatous plaques.	Numerous fibrous areas.	66	M	Salesman and sailor.	Single	Abdominal distention for 4 months; general anasarca; dyspnoea for 1 week (Initial lesion 40 years ago).	+	++++B	+	Cirrhosis of liver.	Ruptured esophageal varix.
14	—	8 cm. Involvement of valves.	Occasional atheromatous plaques.	Occasional irregular gray area	56	M	Printer	Married 21 yrs. 2 children; no miscarriages.	Primary lesion 25 years ago; recent dyspnoea.	+	++++B ++++SF	+	Tabo-paresis	Bronchopneumonia; pyelonephritis.
15	—	Rupture 2 cms. above sinuses	—	Fibrosis	55	M	Cigar maker	Married 29 yrs. 6 children; no miscarriages.	Indefinite dyspnoea and palpitation; mental status confusing.	+	O-B ++++SF	+	Tabes	Progressive circulatory failure with terminal rupture of aorta; pulmonary thrombosis.

16	560	8 cm.; widened & relaxed	Slight atheromatous change.	Fragmented cells; fibrosis & edema	39	M	Manufacturer.	Married?	Initial lesion 15 years ago.	+	?+B ++++SF	+	General paresis.	Circulatory failure complicating malarial therapy.
17	Saved with aorta gross specimen.	8 cm.; dilated; cusps thick; aneurysm of innominate.	Extensive atherosclerosis	Fibrosis; fatty degeneration (tigroid)	64	M	Physician	Married at 35 with 2 children; no miscarriages; again at 55 with no pregnancies.	Dyspnoea for 8 months; orthopnoea for 2 months; general anasarca 1 month.	+	++++B	+	Tabes	Circulatory failure with terminal bronchopneumonia
18	623	10 cm.; extension of aortic involvement.	Luetic involvement of orifices, atherosclerotic plaques	Gumma (?); fibrosis	40	M	Farmer; Moulder	Married 14 yrs. wife died in 1 yr. no pregnancies; remarried 10 yrs. 3 children; no miscarriages.	Sore aching in precordia for 4 months; severe excruciating pain in back to both sides; nocturnal dyspnoea.	+ Aneurysm	++++B	+	0	Progressive circulatory failure, erosion of vertebra by aneurysm.
19	787	9.5 cm.; widened; cusps intact.	Marked atherosclerosis	Hypertrophy, edema and fibrosis	54	M	Cook	Single	Dyspnoea for two years, progressive to orthopnoea; general anasarca.	+	O-B	+	0	Progressive circulatory failure; cerebral hemorrhage
20	305	6.5 cm.	Slight atherosclerosis	Fibrosis	49	F	Housewife	Widow 2 yrs.; Married 19 yrs. 1 child; no miscarriages.	Palpitation and dyspnoea; some edema of ankles	0	O-B ++++SF	—	General paresis (men. vasc. lues)	Rapid circulatory failure
21	470	8.5 cm.; widened orifice; thick cusps.	None	Fibrosis, hypertrophy atrophy & fatty degeneration	34	F	Housewife	Divorced 1 yr. after 4 yrs. married; no pregnancies.	Precordial pain 7½ months; dyspnoea, dependent edema; recent palpitation.	+	++++B	—	0	Infected infarct of lung and bronchopneumonia, rapid circulatory failure

0 Negative or None
— No observation made.

maining four figures having been sacrificed when the gross specimens were kept intact for museum purposes. Of these 17 hearts, 13 were from male subjects and averaged 468.3 grams (range, 250 to 787 grams). Only three of the 13 (250, 280 and 290 grams, respectively) weighed within the accepted normal limits. There were four hearts from female subjects weighing 420.7 grams on an average (range 305 to 470 grams). A single heart, 305 grams, from a female subject was possibly within the normal range.

The aortic ring circumference was recorded in 20 instances (16 males and 4 females). The average from the males was 7.9 cm. with ranges from 6.5 to 10 cms., whereas the aortic ring in the hearts of female subjects averaged 7.8 cms. with a range of 6.5 to 9 cms. Three males and one female showed aortic rings of normal circumference. A casual relationship might be anticipated between the dilatation of the aortic ring and the degree of left ventricular hypertrophy, hence the cardiac weight. By the same token the smaller hearts might be expected in those cases where no dilatation has occurred in the aortic orifice. Therefore, in Table II the extreme weight figures for the two sexes have been taken and the measurements of the respective aortic rings placed in parallel columns.

The lack of close correlation becomes apparent at a glance. In other words there is no direct relationship between the cardiac weight and the size of the aortic orifice. The heart may be grossly hypertrophied without dilatation of the aortic ring. While in general the heavier hearts fall into the group with the wider aortic orifices, enough exceptions are noted to jeopardize any rule. The work of Saphir and Scott,[3,4] in particular, affords the logical explanation for such exceptions in that regurgitation may readily take place through sagging aortic valves whose bases are the seat of syphilitic invasion without actual dilatation of the rings.

In only one instance (case 18) was

TABLE II
COMPARISON OF HEART WEIGHT AND AORTIC RING CIRCUMFERENCE

Case Number	Heart Weight (Grams)	Aortic Ring (Cm.)
	Male	
1	250	6.5
12	280	8.5
13	290	8.
19	787	9.5
6	677	7.5
3	670	8.
	Female	
20	305	6.5
10	465	9.

there involvement of the coronary orifices in the syphilitic process. Sixteen of 20 subjects (one had no note) showed atherosclerosis of varying degrees in the coronary arteries. Macroscopic or microscopic evidences of myocardial degeneration were noted in 17 cases. This figure is conspicuously high; and when the age distribution is considered, its significance will be even more apparent. In one case only (case 18) could histologic evidence of a syphilitic etiology be deduced from the cellular changes in the myocardium.

No detailed discussion of the findings in the aorta is necessary in this connection. The longitudinal striation of the intima and its distribution in the beginning of the aortic arch are important details known to every clinician. If more widespread, the diaphragm almost invariably marks its lowest extension. The nature of the syphilitic involvement of the aortic ring is somewhat less familiar; but its first description by Tripier[8] is exact and his accompanying cut (figure 1) completes the picture:

> Mais ce qui apparait d'une manière très évidente dans la plupart des cas (15 fois sur 20), c'est qu'il existe entre les bords d'insertion valvulaire, contigus à l' état normal, un écartement d'un à plusieurs millimètres que nous n'avons jamais recontré qu'avec une altération de cette nature et qui nous semble dès lors constituer pour elle un caractère pathognomonique.

To the importance of this widening of the commissures between the aortic cusps conclusive observations have been brought by Scott and Saphir,[1,2,3,4,5] who are responsible for the present day appreciation of this detail. Sight must not be lost of the frequent overshadowing of the gross luetic picture by atherosclerosis of the aorta; and as Warthin[9] has pointed out "when the picture is that of atherosclerosis no positive exclusion of syphilis can be made without a microscopic examination." Hence it should be borne in mind that when the gross appearance of the aorta with its atheromatous plaques and ulcerations is most

Fig. 1. Widening of the commissures of the aortic valve (from Tripier).

distinctly atherosclerotic, the necessity for the histologic proof or exclusion of syphilis is even greater than when the appearance is obviously syphilitic. The criteria for a histologic diagnosis of syphilitic aortitis are embodied in the report of case 18 and they have served as the basis for inclusion of all cases in the present series. There is no necessity for reiteration of these details.

Turning to the clinical picture the social history first arrests the attention. There was only one negro in the group. As to age, 18 of the 21 individuals were under 61 years of age and 10 of the group were between 51 and 60 years, inclusive. There were 17 males and 4 females, a ratio of slightly more than 4 to 1. The severity of occupation seemingly bore little relation in predisposition in that 9 individuals followed sedentary work as compared with 12 in laborious trades.

The marital side of the social history was very illuminating. At the time of admission 5 were single; 12 married; 3 widow or widower; 1 divorced. Of the sixteen individuals sometime married, 4 were partners in sterile unions and miscarriages had occurred in 4 other couples. In other words 50 per cent of the married group had procreative disturbances.

The histories afforded but little accurate data relative to the initial lesion. In only four instances was the occurrence of a chancre admitted and the intervals in these cases were widely separated. (12, 15, 25 and 40 years, respectively). Of greater importance in the present relation was the subjective history of these patients with syphilitic aortitis. Dyspnea was the outstanding complaint in 14 and it was apparently a rather late manifestation in the majority of instances. Paroxysmal nocturnal dyspnea does not occur early enough nor regularly enough to be of great help in differential diagnosis; but given the manifestation of sudden starting from sleep with a feeling of choking or of inability to breathe, syphilis of the aorta should receive first thought in explanation. Particularly is this the case when the dyspnea is so severe as to lead to fear of death. Pain was a subjective complaint in only four instances. The low incidence of this symptom is not offered as proof of its inconsequence. As a matter of fact true substernal oppression has a real bearing upon the diagnosis; but anginal attacks and posterior root pains must obviously be related to the special parts involved. Interestingly, case 18 was the only subject to show encroachment of the syphilitic process upon the coronary orifices; yet he escaped anginal attacks. It will likewise be noted that precordial oppression may occur in luetic aortitis in the absence of aneurysms (cases 6 and 10).

The diagnosis of syphilitic aortitis is simplified if aneurysmal dilatation has occurred. Pressure phenomena and characteristic physical signs render the nature and location of such a vascular sac quite exact. These circumstances will account for the diagnosis of four aneurysms of the aorta included in this series. Of the remaining 17, a diagnosis of luetic aortitis was made in 14 from the history and the physical signs without recourse to the labora-

tory. As has been previously pointed out, these cases were late examples of the process. Helpful signs in their recognition included suprasternal impulses, seen or felt, impulses to the right of the sternum in the second interspace, systolic shock by transthoracic palpation, displacement of the cardiac apex down and to the left, widening of the cardiac dullness to the left, supracardiac cap of dullness or dullness under the manubrium, peculiar "bottom of the well" quality to the aortic second sound, systolic slurring with a short rough murmur in the second right interspace transmitted slightly to the vessels of the neck, and ultimately to clear-cut auscultatory evidences of aortic insufficiency without a rheumatic or a septicemic background.

A word further may be offered in explanation of certain of these signs. In palpating for the aortic arch the finger should be placed in the suprasternal notch and then it should be sharply flexed as pressure is made retrosternally. The patient is instructed to flex the neck. In the normal (unemaciated) subject the arch of the aorta cannot be reached by this manipulation; but in syphilitic involvement with loss of elasticity of the aorta, elongation in the long axis is the first response. Hence it is sometimes possible to palpate the arch by this technique before any other sign is demonstrable. (Figure 2). Hoover's[10] suggestion of the bimanual transthoracic palpation for the thrust of the elongated aorta has been largely overlooked. He advised placing the right hand over the right second interspace close to the sternum and the left hand over the left interscapular space. To the palpable impulses which are frequently felt in syphilitic aortitis he applied the terms, systolic shock and diastolic impact. These terms are quite descriptive. However, this simple aid has frequently been neglected. Innumerable qualifying terms have been applied to the aortic second sound in syphilitic aortitis. *Bruit de tabourka* is a favorite; but the Algerian drum is not a familiar musical instrument to most physicians. The tone has always suggested the quality of sound elicited by dropping a pebble into a well; hence the suggestion of a "bottom of the well" sound. The impression gathers with the growing literature on the subject that the profession is seeking a short-cut to the accurate diagnosis of syphilitic aortitis and in the process is neglecting the time-tried and proved methods of physical examination.

The laboratory does have a very important and indispensable place in the diagnosis of syphilitic aortitis. Of these measures the Wassermann reaction suggests itself as the most available. All patients had the Wassermann reaction studied in the blood. The spinal fluid was subjected to this test in 12 cases. Of the 21 specimens of blood tested there were 13 positive and 8 negative reactions, whereas of the 12 spinal fluids there were 9 positive and 3 negatives. A number of combinations suggest themselves; but the most helpful considerations lie in those which offer a check upon the negative blood Wassermann reactions. In 6 cases with negative blood Wassermanns the spinal fluid was studied, and in 3 of these it was

negative and in an equal number, positive. In 2 other instances a low titre in the blood was checked by strongly positive reactions in the spinal fluid. The present series includes a considerable number of individuals with syphilis of the central nervous system, and any evaluation of the relative importance of the Wassermann reactions in the blood and in the cerebrospinal fluid must take this detail into account. Indeed, all of the five cases in which a negative or a faintly positive blood Wassermann was paralleled by a positive spinal fluid, were diagnosed as various types of central nervous system syphilis. Nevertheless, the check of a negative blood Wassermann reaction by a positive return from cerebrospinal fluid is sufficiently common to warrant its consideration.

Increasing importance is being placed upon the fluoroscopic study of the heart and great vessels in luetic aortitis. As pointed out by Kurtz and Eyster,[11] the elongation and the widening of the aorta together with pulsation to the right of the sternum and the visibility of the descending aorta in a subject under 50 years

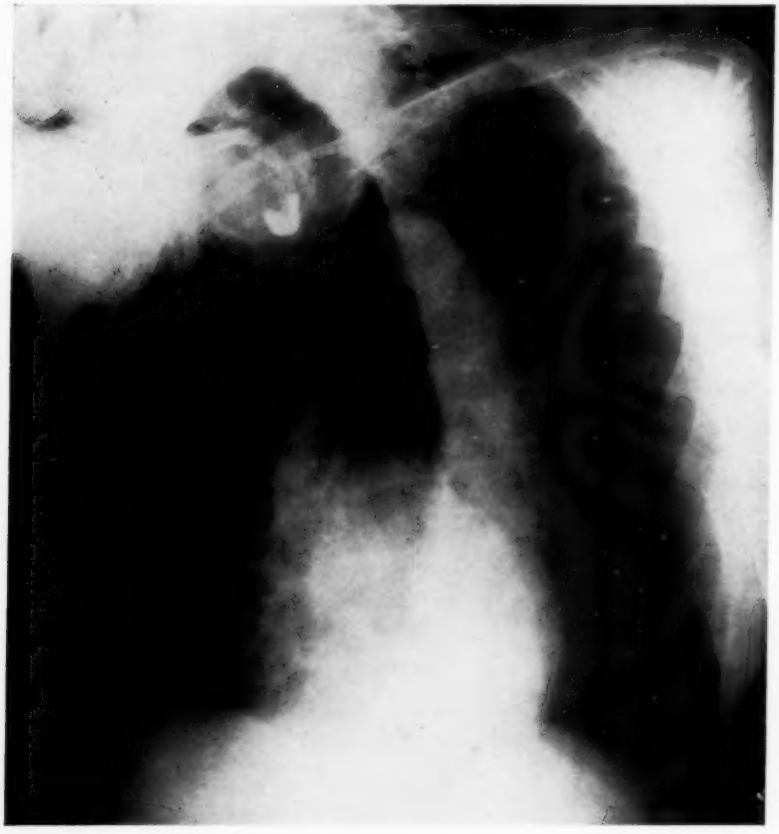

FIG. 2. Roentgenogram showing the position of the finger in retrosternal palpation. Contrast for the finger-tip has been afforded by barium sulphate in a rubber cot.

ge constitute suggestive criteria for the diagnosis of aortitis. Any con-truction of such data into etiologic kground must obviously be pre-umptive; but in principle and prac-e such grounds for the diagnosis of rtitis would appear sound, at least til that stage of life when sclerotic anges make their appearance in the scular bed. Added to the fluoro-opic examination of the aorta itself ould be routine orthodiascopy for liac size and contour. Of some-t less general application and value teleroentgenograms for cardiac and oblique or lateral views for retrocardiac space. If the obvious assistance in the diagnosis of aneurysm in four cases be eliminated from the present discussion, there remain 17 patients upon 11 of whom roentgeno-gic studies were made. In all of se, adequate data were derived om such observations to warrant a onclusion of aortitis. In one instance case 8) a negative cardiovascular agnosis from a clinical standpoint as made positive by roentgenologic udy. Unfortunately the other two gative clinical diagnoses (cases 1 nd 20) were not checked by roent-genologic examinations.

Syphilis of the central nervous sys-em was associated with syphilitic aortitis in 12 cases. This figure is exaggerated in a clinical sense; for only six of this group showed predominant central nervous manifestations. The remaining six cases so classified were diagnosed in part upon neurologic findings of an objective order or by serologic studies on the cerebrospinal fluid. It must be concluded that for this series, at least, the coincidence of syphilis of the aorta and of the central nervous system was very high. One patient (case 13) had syphilitic cirrhosis of the liver.

The manner of death constitutes the final point of clinical interest. Circulatory failure accounted for 10 of the group. Of these the termination was sudden in three and slowly progressive in seven. The next most common method of exitus was collapse succeeding malarial therapy. The occurrence of three deaths attributable to this cause should give pause to the use of malarial therapy in central nervous system syphilis complicated by syphilitic aortitis. The other directly determining causes of death were scattered thus: cerebral accident, 2; broncho-pneumonia, 2; rupture of aneurysm, 1; rupture of aorta, 1; ruptured esophageal varix, 1; melanosarcoma, 1.

Conclusions

Bearing in mind that the group of cases above analyzed represents end-results of syphilitic aortitis in the main, certain conclusions seem justifiable.

1. The diagnosis of syphilitic aortitis in the late stage was relatively accurate by physical methods, abetted by an adequate history.

2. Roentgenologic technique may effect an earlier diagnosis but the etiology cannot be so determined.

3. The Wassermann reaction on blood was positive only in 61 per cent of cases; but further assistance is offered in this direction by the higher incidence of a positive reaction in the cerebrospinal fluid. Hence, a check

of all negative bloods by spinal fluid study may be worthy of consideration where doubt exists as to the etiology of an established aortitis.

4. Most subjects with syphilitic aortitis succumb from circulatory failure. Failing an early recognition and arrest of the syphilitic process, treatment must later resolve itself into an effort to preserve and support a failing myocardium in which apparently an intercurrent coronary sclerosis of non-syphilitic origin is the determining factor in inducing degenerative changes.

5. Malarial therapy imposes a heavy burden upon the myocardium. Accordingly it should be avoided whenever there is evidence of aortitis with aortic valve involvement.

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Bronchomoniliasis: A Clinical and Pathological Study with Report of Illustrative Cases*

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General History

THE history of the higher vegetative organisms began with the work of Hook[1] in the seventeenth century. Saccardo,[1] in 1886, compiled and summarized the information gained up to that time regarding these organisms as pathogenic agents. The revolution in medicine which followed the great discoveries of Pasteur and Koch caused bacteriology to eclipse mycology and only within the last twenty-five years has interest been revived in this important study, due chiefly to Sabouraud, Castellani and Pinoy, and their associates. Castellani has isolated many varieties of monilia and has described the disease entity known as "bronchomoniliasis".

Bronchomoniliasis is a disease of the respiratory organs caused by a fungus of the Genus Monilia. From Ceylon, in 1905, Castellani[1,2] published the first description of this affection and since then cases have been recorded in all climates. From Seattle to Siam, from Baltimore to Buenos Aires come case reports. The only continent from which reports are lacking is Australasia. In 1915, Boggs and Pincoffs[3] reported from Baltimore the first case of pulmonary moniliasis in the United States and since then the disease has been observed from the Great Lakes to the Gulf of Mexico and from the Atlantic to the Pacific, although in the intervening fifteen years only eleven other reports[4] have appeared in our medical literature.

In tropical and subtropical countries bronchomoniliasis is much more common than in the temperate zone, but, masking under the guise of tuberculosis, it occurs in all climates, no doubt, with much greater frequency than is generally recognized. Realization of the cosmopolitian nature of monilia infection, indistinguishable as it is clinically from tuberculosis, will lead to growing appreciation in all parts of the world of the value of prompt recognition of this pathological entity, for, in its mild form, this disease readily responds to treatment with iodides, but, if neglected or treated as pulmonary tuberculosis, it usually ends fatally.

Pathogenicity

Since at present the definite biological relationships between the yeast

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fungi are not settled and fixed grouping for the pathogenic forms is as yet undetermined, some eminent mycologists in this country prefer to concur in the custom, practised abroad, of calling all organisms which produce yeast-like forms in abundance and propagate chiefly by budding, 'blastomycetes' and the diseases produced by them 'blastomycoses', using the terms simply in the generic sense. This terminology is confusing and presents a difficulty to the reviewer, for in the United States the blastomycete is generally regarded as a genus as separate and distinct as the Genus Monilia or the Genus Aspergillus, and in common usage these terms have only a specific meaning.

The Genus Monilia, generally regarded as belonging to the 'fungi imperfecti' or hyphomycetes, is widely distributed in the tropical and temperate zones, and is present in the air, especially of the tropics. It lives in nature in the saprophytic state, thriving on decayed wood, dead leaves, and vegetable debris of all kinds. It may attack any organ or system of the body. Castellani's[5] first investigations were instigated by the constant finding of monilia, in large amounts and without the concomitant presence of tubercle bacilli, in the sputum of persons suffering from a disease entity simulating pulmonary tuberculosis. These persons were employed in tea factories in Ceylon. In the tea leaves and in the tea dust monilia was also found. This initial finding led to studies which have definitely established a large number of species of the Genus Monilia as capable of being the sole causative organism in bronchopulmonary disease. The many varieties are differentiated chiefly by their biological characteristics, especially fermentation of sugars. The types most frequently found in bronchomoniliasis are *Monilia tropicalis* Castellani, *Monilia pinoyi* Castellani, *Monilia metalondinensis* Castellani, and *Monilia krusei* Castellani.

Castellani[6] found that moniliae with the same biochemical properties may differ enormously in their pathogenicity for man and laboratory animals. Species pathogenic to man may be non-virulent to the usual laboratory animals. The vegetative body or thallus of these organisms appears, in its parasitic stage, as a mass of mycelial threads or free-budding forms in the tissues which it invades. Monilia fungi live saprophytically in the human mouth. Parasitically, they attack chiefly the skin and mucous membrane, more rarely the nervous tissue. Bronchopulmonary disease is the most frequent manifestation of monilia invasion. These fungi are not omnipresent but occur in most sputa, and when they appear in large numbers bronchomoniliasis is usually indicated.

Seemingly, the pathogenicity of these organisms in any given case depends largely upon the resistance of the host. In numerous cases a preceding bronchitis, influenza, or pneumonia is mentioned, and in Busse's case, cited by Procházka,[7] pregnancy and childbirth were apparently primary conditioning factors. Procházka believes that most fungi have only a facultative pathogenicity and that a weakened condition of the host's organism (human or animal) may provide the soil

necessary for the development of full pathogenicity. He suggests that sugar-containing media, such as the sugar beet, may increase the pathogenicity of these fungi. From the consideration that monilia grows best in a medium which contains sugar, Balog and Grossi[8] believe that it would more readily penetrate a diabetic terrain and they give insulin in consequence. From the analogy with thrush, of which monilia is the most common causative agent, Kotkis, Wachowiak and Fleisher[9] think it reasonable to interpret bronchopulmonary moniliasis as a condition in which a primary irritating factor, bacterial, toxic or mechanical, initiates changes which permit the fungi to gain foothold, and, once established, to become the essential element in maintaining the irritation.

Etiologic Factors

Most of the cases reported have been in adults, a few suggesting that the infection was contracted in childhood and, after a brief period of activity, lay more or less dormant until middle age. The mode of infection is a matter of conjecture. Undoubtedly, the fungus exists saprophytically in the mouth and may under favorable conditions become pathogenic. Farah[10] and Iacono[1] state that it may be transmitted from man to man. It may be picked up from vegetation, as in the case of the tea factory workers in Ceylon. Balog and Grossi[11] believe that the most frequent carriers of the organism in Egypt are dried fruit and straw, and Mautner[12] calls attention to the frequency of the disease among those having close contact with pigeons and other birds, suggesting their food as a possible source of infection. Since the fungus is prevalent in the air, it no doubt frequently enters the lungs by inhalation. In Ceylon it was found in the nasal cavities of tea-tasters who snuff up tea as well as taste infusions, and Castellani and Chalmers[5] found that guinea pigs into whose nostrils tea dust was insufflated daily for months developed a broncho-alveolar moniliasis. Haberfield, cited by de Almeida and dos Santos,[13] thought that the organism entered by inhalation, and later, writing with Lordy, suggested the tonsils as a portal of entry. De Almeida and dos Santos[13] believe that the organism could travel by the blood stream as well as by the lymph stream.

There are those who agree with Galbreath and Weiss[2] that at present there is no agreement as to what constitutes the Genus Monilia and as to whether it has a primary or a secondary rôle in the etiology of nontuberculous chronic bronchitis. Yet Castellani[1] has grouped the affections due to monilia as follows: (1) Tonsillitis (tonsillo-moniliasis); (2) Bronchitis (broncho-moniliasis); (3) Conjunctivitis (ocular moniliasis); (4) Enteritis (entero-moniliasis); (5) Otitis (oto-moniliasis); (6) Urethritis (urethral moniliasis); (7) Dermatitis (cutaneous and mucous moniliasis). Iacono[1] adds that in certain brain abscesses the cause has been found to be a monilia. Certainly from a nosological standpoint, as Farah[10] suggests, every case of bronchitis, especially every one of long standing, should be well studied and cultures from the expectoration should be obtained.

Symptoms

Primary broncho-moniliasis appears in three forms, i.e., (a) mild, (b) intermediate, and (c) grave. In the mild type the general condition of the patient is good and there is no fever. There is a slight cough with mucopurulent expectoration, often scanty and usually not containing blood. Physical examination of the chest is negative or reveals only a few râles. The intermediate type is characterized by a slight bronchial catarrh and slight fever which is of long duration. The cough, more or less severe, is paroxysmal, occurring morning and night. There may be some degree of dyspnea. In the grave form, the symptoms, the entire clinical picture, and frequently the roentgen picture, closely resemble pulmonary tuberculosis both as to local and general findings. There is the same hectic fever, the gradual and progressive loss of weight, night sweats, and thoracic pain. Cough and dyspnea are severe. There is hemoptysis. The mucopurulent sputum may be of greater or lesser amount. Anemia and emaciation are frequently pronounced. On chest examination, there may be found areas of dulness with increased or diminished tactile fremitus due to consolidation or pleural thickening; bronchial or bronchovesicular breathing, or the breath sounds may be entirely absent; a few inconstant fine crepitations or many moist râles as well as an occasional pleuritic rub.

The course of the disease may be acute, but usually it is prolonged, with remissions and exacerbations, terminating in gradual deterioration or gradual recovery. Some of the intermediate types present the physical signs of chronic bronchitis rather than of pulmonary tuberculosis. Others present the clinical picture of bronchial asthma. In a number of cases, occurring in different parts of the world, the course has been described as resembling pneumonia. Thus, rigors with high fever are mentioned in a few cases, and in several cases of acute onset the temperature fell by lysis after from eleven to fourteen days, convalescence following. Occasionally, sore throat and huskiness of voice appear as early symptoms. In one or two cases, inflamed tonsils are mentioned. Intense dyspnea is not infrequently noted. Balog and Grossi[11] ascribe the dyspnea and cyanosis in some cases to the accompanying myocarditis and decompensation of the right heart, which they attribute to the toxins of the monilia. These authors also mention pains in the lower limbs in cases of long duration.

The cough is paroxysmal, usually worse at night and in the morning. The sputum is sometimes scanty and difficult to raise, sometimes abundant. Except in the mild type of the disease, it is likely to be blood-streaked. It has been described as "like milk", later becoming curdly and pinkish, and again as grey, lumpy and gruel-like with a yeast-like taste. An odor is sometimes present in the breath, variously described as "like yeast" and "like beer fermentation". Castellani[14] remarks that the sputum may have an odor resembling that of commercial yeast. In examining sputum containing *Monilia metalondinensis*, Wheeler and Hoffstadt[15] detected a yeast-like odor after a short period of incubation.

Diagnosis

The diagnosis cannot be made at the bedside. It is based on (a) finding the fungus—yeast-like cells, more rarely mycelia—in the sputum, and (b) by culture. The species is determined by the specific fermentation of various sugars. The first essential is to obtain the sputum as fresh as possible after the patient has washed his mouth thoroughly with boiled or sterilized water. Castellani[14] emphasizes the importance of having the patient gargle and rinse the mouth with sterile salt solution before being asked to cough or expectorate, because of the frequency with which the monilia fungi exist saprophytically in the mouth. He also stresses the necessity of immediate examination of the specimen in order to avoid air contamination.

Primarily, the diagnosis rests on the absence of tubercle bacilli and the presence of moniliae in the sputum, but cultural investigation and animal inoculation are also necessary. Castellani, Douglas and Thompson[6] warn that a definite diagnosis of primary bronchomoniliasis should be made with great care and only when the bronchial expectoration, collected with every possible precaution, contains monilia in fair amount, tubercle bacilli being absent, and when the number of organisms decreases rapidly with the gradual improvement of the condition. Tuberculosis is excluded by the skin reaction, repeated absence of acid-fast bacilli in the sputum, and the biological tests. Syphilis and bronchial spirochetosis are excluded by serological tests and by examination for spirochetes. Other fungi are to be considered and looked for in cultures.

Animal inoculation, according to Castellani,[14] provides the conclusive step. His criterion is that intrapulmonary injection into a rabbit must induce the characteristic numerous small white nodules, containing the fungus, in both lungs. It is not sufficient that an injection into the peritoneum or vein produce death in the animal with pneumonia and general septicemia; the strain present in the sputum must be shown to be capable of producing the characteristic lesions in the lungs. In the published cases of bronchopulmonary moniliasis this condition does not appear to have been fulfilled very generally. Some authors do not regard animal inoculation as essential to a final diagnosis.

Balog and Grossi[5] reported testing eighteen patients who had pulmonary moniliasis, using scarification tests and intracutaneous and subcutaneous inoculations. Using as antigen an emulsion of the fungus killed by heat, they obtained only a general reaction which they interpreted as nonspecific. Thereafter, they employed emulsions made from living, untreated *Monilia pinoyi* Castellani which, they state, is strongly pneumotropic and does not harm the host when inoculated into the skin. With this living antigen intracutaneous inoculations were positive in all eighteen of the patients with pulmonary moniliasis and negative in all of the fifty-three controls consisting of normal healthy individuals or persons suffering from tuberculosis or other disease not due to monilia. The scarification tests were not successful, although intracutaneous tests, made simultaneously in the same patients, were positive. In Steinfield's[16] study

of fifteen cases of bronchomycosis associated with certain types of bronchial asthma, intracutaneous reactions could not be interpreted.

Differential Diagnosis

Differentiation from tuberculosis is as difficult as it is important. Mere absence of tubercle bacilli from the sputum is in itself not conclusive. The guinea pig inoculation test for tuberculosis must always be made. Roentgen examination is also important and should never be dispensed with, even though it serves only to rule out pulmonary carcinoma. It appears to be fairly characteristic of the roentgen picture in primary bronchopulmonary moniliasis that the apices remain clear; otherwise, the roentgenogram may correspond to that of tuberculosis in its various stages.

Frequently moniliae and tubercle bacilli are found together in the sputum. In that event, the monilia may be a saprophyte or there may be a true double infection. Balog and Grossi[8] mention three cases in which they found that the symptoms clearly indicated the presence of the two diseases. They regarded the condition as a genuine moniliasis engrafted on a tuberculous base. Many writers on the subject look upon the fungus as a secondary invader when it is associated with the tubercle bacillus. A large number even assume that it may be disregarded from the therapeutic standpoint. That the fungus, appearing in abundance soon after infection, may antedate the tubercle bacillus in the sputum by months is not deemed significant of its priority as a causative agent. In general, once the tubercle bacillus has appeared, it is assumed that it represents the primary infection and bronchopulmonary moniliasis is assigned a secondary rôle.

The opinion, however, that the fungus infection is frequently the primary disease is not without supporters. Some feel that the ensuing pulmonary deterioration provides suitable soil for the subsequent lodgment of the tubercle bacilli. In support of this view Marett's observations are of interest. Ferguson[17] cites Marett as saying that, in the Channel Islands, monilia infection of the lungs is as frequent as tuberculosis, and that most patients with tuberculosis have the double infection. Marett found "blastomycetes" alone in forty per cent of cases of suspected tuberculosis, "blastomycetes" and tubercle bacilli in forty per cent, and tubercle bacilli alone in twenty per cent. His experience led him to conclude that patients of the first class, if left untreated, soon pass into the second, a damaged lung being particularly susceptible to tuberculous infection, and that this second group has an outlook less hopeful than that of the third group who have only the pure tubercle bacillus infection. In order to avoid mixed infection in patients who have tuberculosis only, he urges their isolation from patients who have fungi as well as tubercle bacilli in the sputum. He finds that all cases of true double infection do best by treating the monilia infection first and then proceeding with the tubercle bacillus vaccine. In this, Balog and and Grossi[8] agree with him. Craik,[18] who cites Marett's observations in connection with his own report of a case of bronchopulmonary moniliasis,

says: "I think it probable that Colonel Marett has brought to light a truth unsuspected by his predecessors—that chronic blastomycetic bronchial catarrhs occur frequently and that they are the commonest precursors of tuberculosis in this country (England)."

The following is an illustrative case:

M. B., aged 56, a merchant, first consulted the author in December, 1923, because of fever, cough, dyspnea, and pain in the chest.

Past History: Ten years before, he had had an attack of "pneumonia" and was confined to his bed for three months. Thereafter, he had had one or more attacks of "bronchitis" each winter. Tuberculosis was suspected each time, but in no instance were tubercle bacilli found in his sputum.

Present Illness: The attack which began late in 1923 kept the patient in bed for a little more than one month. In addition to cough, dyspnea, and a pleuritic type of pain in the left chest, there was an irregular temperature ranging from 99° to 103°. The cough was paroxysmal and there was profuse expectoration of a yellowish mucoid material, occasionally blood-streaked. The respiration was rapid, varying from 30 to 40 per minute. The pulse rate ranged from 110 to 120. Examination of the chest revealed a leathery pleuritic friction sound over the entire left chest. Many moist râles were heard over both lungs, but were most numerous over the lower half of the left. Resonance was impaired, especially over both lower lobes, the impairment being somewhat more marked over the left. Several examinations of the sputum were made. All were negative for tubercle bacilli but *Monilia pulmonalis* was found each time, both on direct smear and in culture. An x-ray examination of the chest (see figure 1) showed extensive infiltration throughout both lungs, more marked on the left with both lower lobes especially involved. Iodide treatment was instituted and at the end of six weeks the patient was able to return to his business. He was, however, still short of breath on slight exertion and continued to have paroxysms of coughing.

Clinical Course: He was not seen again for eighteen months. At that time he was having another attack of "bronchitis" similar in every respect to the one just described. The sputum was again negative for tubercle bacilli but *Monilia pulmonalis* was readily demonstrated as before. X-ray examination (see figure 2) now showed a diffuse infiltration of both lungs as before, but with considerably less involvement of the left lower lobe. The amount of lung involvement, on both examinations, was out of all proportion to the patient's symptoms and general appearance. The blood examination showed the following: Hemoglobin, 75 per cent; erythrocytes, 4,400,000; leucocytes, 8,150; polymorphonuclear neutrophiles, 76 per cent; lymphocytes, 24 per cent.

Six months later, the patient had another attack which began in every respect like the many previous ones. There was the usual fever, pain in the chest, dyspnea, and cough with rather profuse expectoration. After a few days, areas of consolidation were found in the lower lobes of both lungs. Respiration became very labored and marked cyanosis appeared. The sputum contained considerable blood and was more tenacious than usual. Surprisingly enough, examination of the sputum showed many tubercle bacilli and many pneumococci. No moniliae were found in direct smear but they were grown in culture as before. The patient died at the end of two weeks, apparently from a bronchopneumonia. An autopsy was refused.

In such cases as this it is, of course, impossible to determine definitely which infection preceded. In this particular instance, however, it seems only reasonable to assume that there was a genuine primary moniliasis which provided suitable soil for the later invasion of the tubercle bacilli, the bronchopneumonia serving merely as a terminal event.

Balog and Grossi[8] emphasize one important point of differentiation be-

tween primary pulmonary moniliasis and the secondary form accompanying tuberculosis. Cases of primary moniliasis of the lungs always show lesions of the base while lesions at the apex of the lungs, or extending to the apex, are identified as mixed forms of tuberculosis and moniliasis, the mycosis being regarded as a secondary infection. A second point of differentiation is that in secondary moniliasis, the mucous membranes of the mouth, pharynx, and bronchi are usually invaded by the fungus. This is very rare in the primary type of lung infection.

In addition to a symbiotic action between monilia and the tubercle bacillus, other cases of mixed infection of the lungs have been reported. Secondary bronchomoniliasis is not infrequently met with in such cachectic

FIG. 1, Case 1, M. B. (Dec., 1923). Showing infiltration of both lungs, more extensive on the left, and especially marked in the lower lobes.

diseases as cancer and diabetes. Monilia finds sugar-containing media particularly desirable soil.

The following case of pulmonary moniliasis occurred in a patient who also had syphilis. The relation between the monilia infection and the syphilis was always problematical.

W. W., male, aged 41, first came to the clinic in December, 1923, complaining of shortness of breath, cough and weakness.

Past History: For fifteen years he had been troubled off and on with cough, much wheezing, and dyspnea on exertion. For three years these symptoms had been continuous. Occasionally he had had fever for several days at a time, and a few times the sputum had contained blood. Nevertheless, he had gained twenty-five pounds in weight. For several years he had been having hay fever with attacks of asthma, commencing in August and continuing until frost. Aside from his pulmonary symptoms his general health had been good. There was a fairly definite history of

FIG. 2. Case 1. M. B. (May, 1925). A diffuse infiltration of both lungs still present but a decided clearing of the left lower lobe.

syphilis, but he had considered himself cured.

Present Illness: At the time of consultation the patient related that the cough, wheezing and dyspnea, which had troubled him continuously for three years, were steadily growing worse and were accompanied by an increasing weakness. He had the appearance of a robust middle-aged man weighing about 200 pounds. His breathing was somewhat labored and examination of the chest revealed a moderate lagging of the left side with greatly impaired resonance over the left base. Many moist and wheezing râles were heard over the lower half of both lungs, more on the left than the right. The heart sounds were obscured by the wheezing but were apparently normal. The blood pressure was 110/85, the pulse 86, and the respiration 24. The blood count was as follows: Hemoglobin, 90 per cent; leucocytes, 9,150; polymorphonuclear neutrophiles, 68 per cent; lymphocytes, 32 per cent. The blood Wassermann was four plus positive. Urinalysis was essentially negative. Several sputum examinations were negative for tubercle bacilli. No cultures were made at this time.

Roentgenological examination of the chest (see figure 3) showed the left lung about

FIG. 3, Case 2, W. W. (Dec., 1923). The left lung is about fifty per cent collapsed with multiple adhesions between visceral and parietal pleurae resulting in the formation of many pneumothorax pockets. Also an area of consolidation in the right cardiophrenic angle.

fifty per cent collapsed with multiple adhesions between the visceral and parietal pleurae, resulting in the formation of many pneumothorax pockets. There was no free fluid, but there was an area of consolidation in the right cardiophrenic angle, with some mottling throughout the right upper and middle lobes giving the appearance of pulmonary tuberculosis. The heart and mediastinum were displaced to the left.

Clinical Course: Because of the unusual lung findings, the negative sputum, and a strongly positive Wassermann, a tentative diagnosis of syphilis of the lungs was made and an intensive course of antisyphilitic treatment was commenced. Sulpharsphenamine, salicylate of mercury, and iodides were employed alternately. A month later the patient reported that he was much improved, was coughing less, and had less dyspnea. Three months after treatment had begun his general condition was greatly improved but there was no appreciable change in the pulmonary condition either on physical or x-ray examination. The sputum was again negative for tubercle bacilli and the blood Wassermann was still four plus positive.

After two months more of antileutic treatment he was coughing more and expectorating large amounts of yellowish purulent sputum, occasionally blood-streaked. He was having an irregular temperature, at times reaching 102°. He also complained of frequent attacks of a pleuritic type of pain in the right chest. The sputum was now cultured for the first time for possible fungi and *Monilia pulmonalis* was grown in large numbers. During the next twelve months, in addition to the routine antiluetic treatment he was given iodides in large doses, both by mouth and intravenously. Under this treatment there was less cough and expectoration, less dyspnea, and a considerable gain in strength. The treatment was continued intermittently and about a year later the roentgenogram (see figure 4) showed that some re-expansion had occurred in the left lower lobe and in the base of the left upper with a diminution in the size of the pockets of pneumothorax. The left lung was still very poorly aerated, showing many areas of increased density, probably fibrosis. No change was apparent in the right lung. Three months later, examination showed continued improvement but there was one large area of pneumothorax present in the left apex reaching down to the level of the second rib anteriorly. Still no change was seen in the right lung.

In the meantime, several sputum cultures had been made and the monilia was recovered each time. Finally, an autogenous monilia vaccine was given over a period of two months with no apparent benefit. The patient now passed into the hands of another physician who states that for the next three and one-half years the patient's condition was essentially unchanged and that, in spite of the cough and dyspnea, he was able to carry on his work as a traveling salesman. Several sputum examinations were made for tubercle bacilli, all of which were negative. In December, 1929, he developed influenza to which he succumbed in three days.

Mixed infections with two different fungi are occasionally met with. Cases of mixed monilia and anaeromyces infection have been described by Castellani, Douglas and Thompson,[6] and of monilia and spirochetes by Castellani[14]. They base their belief that each was playing an etiologic rôle on the cure obtained by combining the treatments for the two conditions after treatment for each separately had failed. They suggest that when a mild or moderately severe case of bronchomoniliasis fails to respond to potassium iodide and creosote, mixed infection should be considered and a second organism looked for.

Cases of bronchitis and bronchial asthma, pneumonia, pseudodiphtheria, cancer of the lung, phthisis, tuberculosis of the axillary lymph glands, glycosuria, diabetes, bronchospirochetosis, anaeromycosis, thrush and dermatitis have all been mentioned in which a more or less important rôle is ascribed to monilia. In its primary

form bronchopulmonary moniliasis should be promptly differentiated, especially from tuberculosis. Even when secondary, it should not be neglected, for it only prolongs the course of the original process and causes further damage.

Clinical Pathology

The moniliae belong to the family of hyphomycetes. There are many varieties. Castellani[1] alone has isolated more than forty species and others have added to this number. The Genus Monilia is characterized by sporophores which are simple or subsimple and proceed by constriction at their extremities, and by a chain of large lemon-shaped conidia often provided with a disjunctive apparatus. The tendency has been, however, according to Castellani, Douglas and Thompson,[6] to include under the term "monilia" all the organisms of the family Oosporacea Saccardo, 1886. The lack of definitely fixed biological re-

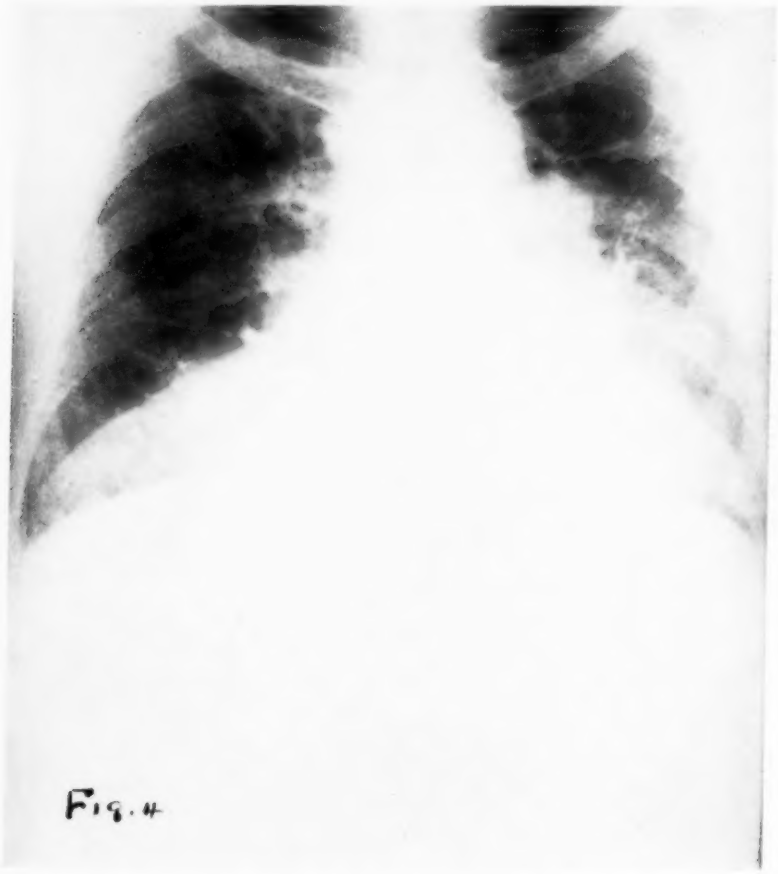

Fig. 4, Case 2, W. W. (May, 1925). Some re-expansion had occurred in the left lower lobe with a decrease in size of the pneumothorax pockets except the one at the apex. No change was apparent on the right.

lationships in the field of the yeast fungi has been mentioned in a foregoing paragraph. When isolated from lesions monilia presents microscopically a vegetable body composed of mycelial filaments of somewhat large size, frequently having arthrospores and numerous free oval or somewhat round "buttons". When grown in cultures, especially on solid media, the organism consists exclusively of oval or somewhat round "buttons". It grows well on solid or liquid media containing glucose or maltose.

In making cultures the greatest care must be exercised to exclude the ordinary saprophytic mouth fungi. Castellani's[14] method is to cleanse the mouth with a wash of a 1:5000 solution of potassium permanganate. The patient then expectorates into a sterile Petri dish. The sputum is inoculated on plain broth, agar and glucose broth. These are incubated at room and incubator temperatures. At the same time, the sputum is examined for protozoa and tubercle bacilli. After forty-eight hours, white colonies, milky in appearance with "cupola" tops, are selected and examined microscopically. The presence of conoid forms about the size of a red blood corpuscle confirms the presence of some species of monilia. Passing the culture through a series of sugars completes the classification of the parasite.

Identification of monilia in direct smears of sputum is by no means easy unless the fungi are present in very large numbers. Pijper[19] finds the resemblance of the oval spores to the nuclei of body cells or even chromocytes very misleading. He mentions a differential stain which he has found highly satisfactory. In examining the fresh sputum, spirochetes are ruled out by means of dark ground illumination, lung parasites, such as *Paragonimus ringeri* (Cobbold, 1880), by simple microscopical examination, and tubercle bacilli and the acid-fast species of Nocardia are distinguished by one of the usual methods of demonstrating acid-fast bacilli. The presence of non-acid-fast species of Nocardia and of yeast-like fungi is revealed by coloring films of the fresh sputum by Leishman's and Cram's methods.

The blood findings vary considerably, many investigators finding no important changes in the blood picture while others report marked variations. Some degree of anemia appears to be the rule. A slight leukocytosis has been mentioned a few times, and eosinophilia is frequent.

Complement fixation reactions with the sera of patients have been obtained in some instances, notably in the cases reported by Farah,[10] Kurotchkin and Chu,[20] and Hoffstadt and Lingenfelter[21]. Steinfield[16] found the complement fixation reaction of equivocal value, and concluded that the agglutination reaction gave no new information. Peruchena's[22] agglutination experiments with normal and immune sera were negative. In Parise's[23] case the organism was not agglutinated by the patient's serum. Farah,[10] however, found that the fungus gave a positive agglutination reaction with the patient's serum, and Hoffstadt and Lingenfelter[21] noted that this organism showed spontaneous agglutination. A positive precipitin reaction was obtained by Kurotchkin and Chu[20] when the patient's serum

was added to various extracts of monilia cells, and control sera were negative. Peruchena's[22] attempts to produce hemolysis with cultures failed.

Roentgen examination is of value in all cases. It shows definitely the location of the infection and its progress. A general characteristic of genuine primary bronchopulmonary moniliasis is that the apices remain clear, even in advanced cases. The x-ray also serves to rule out pulmonary carcinoma, and when used in conjunction with lipiodol injections, to exclude bronchiectasis.

Very few postmortem examinations have been reported. A review of the literature on bronchomoniliasis reveals only five authors[24] who mention autopsies. The only report of a postmortem examination made in the United States appeared from Baltimore in 1916 when Boggs and Pincoffs[3] described the first case of pulmonary moniliasis published in medical literature in this country. The case report appearing at the conclusion of this paper contains a detailed account of the postmortem findings in the author's case of primary bronchopulmonary moniliasis in which *Monilia pulmonalis* was demonstrated repeatedly in the sputum, both on direct smear and on culture. Repeated examinations for tubercle bacilli were always negative.

Pathology in Experimental Animals

Castellani[14] found that the virulence of different moniliae varies: i.e., (a) a few strains are non-virulent to laboratory animals; (b) certain ones are virulent and will kill a rabbit or a guinea pig following intravenous or intrapulmonary inoculation, but without the evident pseudotubercular nodular condition of the lung; (c) others produce a peculiar nodular condition both in the inoculated and in the non-inoculated lung, when injected intrapulmonarily and at times intravenously.

If the monilia isolated from the sputum is nonpathogenic, intrapulmonary inoculation in rabbits produces neither lung lesions nor general infection. When the fungus is virulent but only a secondary invader, intravenous injection will kill the rabbit and intrapulmonary injection will induce a fatal septicemia, but without a localized nodular affection of the lungs. When the monilia is the real cause of a broncho-alveolar condition, intrapulmonary injection will produce in the rabbit a very characteristic nodular condition of the lungs, both lungs becoming studded after two or three weeks with a large number of white nodules which contain the fungus. Some of these nodules may coalesce, forming a staphyloid mass. The smaller nodules are about one-eighth of an inch in diameter and microscopically, contain in their centers masses of small white cells and polymorphonuclear leukocytes which decrease in number peripherally. They are in turn surrounded by a ring of epithelial cells, many containing phagocytized smaller white cells, together with a few large multinucleated giant cells. At times the cells in the center of the nodules are markedly degenerated, the nodules there showing gross caseation. In most instances there is some congestion but no pneumonia between the nodules. Thickening of the intima is present in the small arteries.

Castellani[14] maintains that the demonstration of the characteristic nodular condition in the lungs is essential for the establishment of the diagnosis of primary bronchopulmonary moniliasis, while other writers contend that animal inoculation is not even necessary when the sputum is repeatedly positive for monilia.

In their animal experiments, Balog and Grossi[3] used an emulsion of living mycetes. Intrapulmonary inoculation, as first done by Castellani, they found to be the most efficacious method of injection. They give an excellent description of the lung changes following intrapulmonary inoculation into rats of a strain capable of producing pulmonary disease, and note the remarkable likeness to tuberculosis. Intracardiac inoculation into guinea pigs resulted in death from acute septicemia. Kurotchkin and Chu[20] found that intrapulmonary inoculation of *Monilia tropicalis* did not kill the rabbit in from three to five weeks, but invariably produced extensive necrosis in the lung with obliteration of the pleural cavity and formation of a few nodules. Intravenous and intraperitoneal inoculation killed with mycotic septicemia, small disseminated whitish nodules containing the monilia appearing in the lungs and other organs. In general, intravenous inoculation with a virulent strain produces general septicemia; nodules may appear in various organs, with or without simultaneous lung involvement. Intraperitoneal inoculation may or may not succeed.

Prognosis

The mild type of bronchomoniliasis may result in spontaneous cure and is always readily amenable to specific treatment. Usually the intermediate type also yields to treatment, but the response is slow. A prolonged course of treatment is often necessary. Sometimes this type apparently remains stationary, but, if neglected, it not infrequently passes into the severe form. Except perhaps in its early stages, the severe type is usually incurable, although death may not take place for many months.

Chyrulia[25] presents from Venice a good example of the chronic intermediate type of the disease. A more severe form which, nevertheless, seems to have changed little over a period of ten years is described in detail by Galbreath and Weiss[2] from Porto Rico. Colard and Jaumain[26] of Belgium describe a case which presents the progressive type. In one of five cases, reported by Stovall and Greeley[27] from Wisconsin, the course was rapid, death ensuing in four weeks. This case appears to have been of the severe type from the beginning. The case report which appears at the conclusion of this article illustrates the severe type of the disease.

Treatment

The treatment of bronchomoniliasis is based upon the specific germicidal effect of potassium iodide on monilia. This drug has had such beneficial effect, particularly in the mild and intermediate cases, that it has come to be regarded as the specific. In severe cases, however, it appears to be of little, if any, value. In such cases lipiodol by intratracheal injection deserves extended trial. This may be combined with intramuscular injec-

tions. Castellani[6,14] advises that potassium iodide be given in fifteen grain doses in milk or water three times a day, this treatment requiring three or four weeks to effect a cure in mild cases. In addition, he advises creosote, glycerophosphates and balsamics, and tonics to combat the loss of appetite and the anemia. He has found that cases of mixed infection, as for example moniliasis and anaeromycosis, are frequently cured by combining the treatments for the two infections. When possible, the patient who lives in a hot moist part of the world should be removed to a more suitable climate.

Stovall and Greeley[27] treated one case with intravenous injections of gentian violet, and saw much improvement. Balog and Grossi[8] believe that insulin is of value, even in cases without glycosuria. Farah[10] states that pneumosan injections may prove useful. He recommends lipiodol—forty per cent iodine in poppy oil—(2 cc.) injected intramuscularly in the gluteal region on alternate days, as this treatment appears to be useful in early stages before there is serious damage to the lungs. Energetic treatment, using "iodides, autovaccine (Steinfeld's method), alkalines by mouth, ultraviolet rays, etc.", produced good results in the chronic case Chyurlia[25] reported from Venice. In Nasso's[28] case of a child who had previously had malaria, despite a negative search for plasmodia, the patient improved under intensive quinine treatment. Craik[18] treated his patient successfully with alkalis, potassium iodide, and adrenalin.

In their case from the Belgian Congo, which had progressed rapidly and was in an advanced stage when the patient came under their observation, Colard and Jaumain[26] used injections of oil containing iodoform, eucalyptus, and creosote, and intravenous injections of sodium cacodylate and potassium iodide by mouth, all without result. Because of respiratory difficulties artificial pneumothorax had to be discontinued, and because of the venous sclerosis induced, intramuscular injections of Lugol's solution, 6 cc. per day, had to be substituted for the intravenous injections. Local applications to the buccopharyngeal lesions were powerless to check their advance. All treatment was unavailing.

Satisfactory results from small doses of roentgen rays in ten cases of bronchomycosis have been reported by Howe and Schmidt,[29] but they do not state the kind of fungus involved. Among their patients were two bakers, each having considerable yeast in the sputum. Both were helped by x-ray treatments.

Vaccine treatment has had varying success. Of the forty-three cases Pijper[19] mentions, sixteen were treated with autogenous vaccines only, the doses ranging from fifty million cells to two thousand million cells. Very good results were obtained in three cases and there was distinct improvement in three others, but in the remaining ten cases there was no improvement. This author believes that iodine should be given in addition to the vaccine. Kotki's, Wachowiak and Fleisher[9] saw complete disappearance of symptoms following the use of autogenous vaccine in one case, and great improvement in another before it passed out of control. In Steinfeld's[16]

fifteen cases, iodides were efficacious and vaccines, prepared from organisms killed by heat, dose 0.1 cc. increasing to 1.0 cc., seemed to help. For therapeutic purposes Balog and Grossi[11] used the same emulsion of living, untreated *Monilia pinoyi* Castellani as for diagnostic skin tests. By repeated injections with progressively increasing doses, they were able to effect healing in a short time in most cases and to produce great improvement in the remainder. They note that monilia vaccine therapy always acts gently and that desensitization takes place during the treatment. They have found vaccine treatment the only therapy which restores the myocardium after injury by the monilia toxins.

Case Report with Postmortem Findings

Mrs. J. H. T., aged 38, the mother of four healthy children, the youngest five years of age, first consulted us in October, 1923, because of fever, cough, and occasional hoarseness.

Family History: The family history was negative.

Past History: The patient had lived in Memphis for the preceding eleven years; prior to that she had lived in Virginia and in Washington, D. C. She had influenza during the epidemic of 1918 and typhoid fever in 1919. In 1920 she had an attack of pleurisy with effusion, apparently with complete recovery. The chest was aspirated at that time but no bacteriological examination of the fluid was made. The following spring (1921) she had a second attack of pleurisy for which she consulted a well known internist in the East who diagnosed pulmonary tuberculosis although sputum examination was negative for tubercle bacilli. Within a few weeks she was free from fever and for the next eighteen months considered herself well.

Present Illness: During the early spring of 1923 she began to complain of cough and hoarseness, and a few times expectorated blood-streaked sputum, but she did not consult a physician. Her weight had remained practically stationary since the attack of typhoid fever four years before, but there had been a noticeable lack of endurance and some shortness of breath on exertion. It was of these symptoms as well as of cough, hemoptysis, hoarseness, and slight fever that she complained when she first consulted us. There were no digestive or urinary symptoms. Her menstruation was normal and regular.

Physical Examination: The patient was a well developed and well nourished middle-aged woman weighing 160 pounds. Her color was normal and she did not look ill. The tonsils were somewhat enlarged and showed evidence of chronic infection. The general physical examination was otherwise essentially negative except for the chest findings.

Chest: Expansion of the left side was diminished. Over the lower part of the left upper lobe and over all of the left lower lobe there was marked dulness and decreased tactile fremitus. Over this area there were moist râles and diminished breath sounds. Both apices were apparently clear but there was an area of dulness without râles in the right axilla. There were no areas of tenderness to pressure.

Heart: The apex beat was neither visible nor palpable. The area of cardiac dulness blended with that of the lung dulness. The heart sounds and rhythm were normal. The blood pressure was 120/80, and the pulse 82.

Clinical Course: In spite of a negative sputum examination we concurred in the previous diagnosis of pulmonary tuberculosis and considered it of the fibroid type. A few weeks later the patient entered a well known tuberculosis sanatorium in North Carolina where she remained for eight months. While there her temperature remained normal except for an occasional slight rise following an injection of tuberculin. Her cough and hoarseness practically disappeared and she gained several pounds in weight. During her stay in the sanatorium repeated sputum examinations were

made for tubercle bacilli, all of which were negative. No other bacteriological studies were made. In spite of this clinical improvement x-ray examination showed a definite increase in the area of infiltration in the lungs.

The patient returned to Memphis on July 4, 1924. She looked and felt well. The next day she had a rigor followed by temperature of 103°. In a few hours there developed a pain of pleuritic type in the left chest posteriorly. The following day she was coughing considerably and the sputum was streaked with bright blood. Examination of her chest showed marked dulness throughout the left lung from the level of the third rib to the base, with diminished breath sounds and tactile fremitus. Moist râles were heard over both lungs but there were more over the left than the right and more over the lower than the upper lobes. Respiration was 36 and the pulse

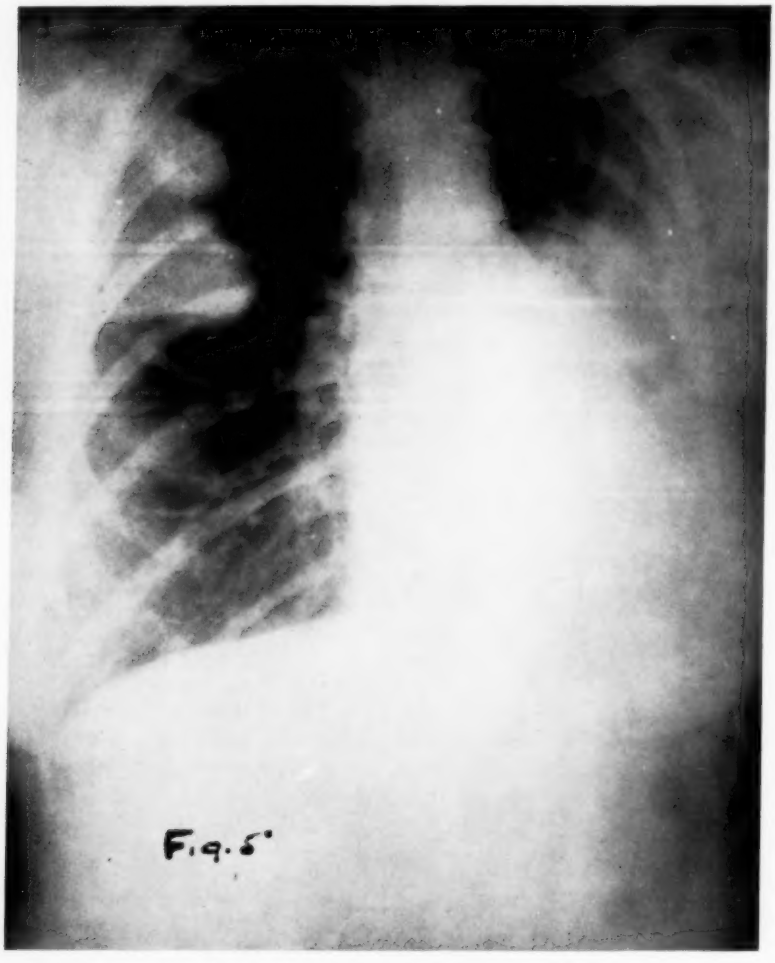

FIG. 5. Case 3. Mrs. J. H. T. (Oct., 1923). Showing a marked homogeneous density involving the lower half of the left lung with the mediastinum displaced to the left. In the periphery of the right lung are two areas of similar density, roughly triangular in shape with bases at the periphery and apices toward the center of the lung. Both apices clear.

was 120. For the next ten days she was critically ill; her temperature ranged from 100° to 103°. At the end of two weeks the temperature was normal in the mornings but continued to rise in the afternoons to 101°. The dulness over the left base increased and a possible pleural effusion was suspected. The chest was aspirated but nothing was obtained. The sputum was persistently negative for tubercle bacilli. The total and differential blood count remained normal.

Two months later the general condition of the patient showed very little change. She was still having an afternoon temperature, and the cough and the quantity of expectoration had increased. She had apparently gained in weight but was becoming more dyspneic and had to sleep most of the time on three pillows. She was most comfortable when lying on the left side. Chest examination now showed considerable dulness and more moist râles over the right lower and middle lobes. The right upper lobe and the upper half of the left upper lobe remained apparently clear.

In the meantime, repeated cultural studies of the sputum for fungi had been made and each time there was obtained a pure growth of *Monilia pulmonalis* Castellani. Convinced that we were not dealing with tuberculosis, we commenced the administration of iodides in large doses, at first by mouth and later intravenously. The only noticeable effect of this treatment was a marked increase in the quantity of sputum, in which an occasional streak of blood continued to appear. Sodium cacodylate was then tried, both intramuscularly and intravenously, but to no avail.

Finally, with both lungs apparently solidified except the right upper lobe and the apex of the left upper, the dyspnea was so great that the patient was compelled to sit upright to breathe. There was considerable cyanosis and a moderate amount of subcutaneous edema. The temperature continued to range from 99° to 101°, the pulse and respiration gradually increasing. But, withal, there was no apparent loss of weight and but little anemia. Death occurred on December 24, 1924.

Roentgenological Findings: The first x-ray examination, made October 2, 1923 (see figure 5), showed a marked and fairly homogeneous density throughout the left lower lobe which blended with the heart shadow. The mediastinum and the heart were displaced to the left. The upper margins of the density were fringy and invasive in appearance. In the periphery of the right lung there were noted two areas of similar density, both roughly triangular in shape with bases at the periphery and apices toward the center of the lung field; the upper and smaller area seemed to be situated in the lower part of the upper lobe, while the larger area seemed to be in the adjacent part of the lower lobe. The apices of both lungs were strikingly clear.

Five weeks later (see figure 6), the areas in the right lung had increased in size and were becoming more confluent. The density in the left lung had extended upward, especially at the periphery. No new areas were noted. Seven months later (see figure 7), the heart and mediastinum were displaced further to the left and the upper lobe was so encroached upon, both from the mediastinum and from the invasion below, that only a small portion appeared to be air-bearing. The two coalescing areas in the right side now extended from the periphery to the mediastinum and seemed to involve all of the middle lobe as well as the lower part of the upper lobe. That part of the shadow corresponding to the lower part of the upper lobe showed a lighter central area suggesting cavitation. Several new small areas of density now appeared in the right lower lobe.

The last x-ray examination was made October 2, 1924 (see figure 8), exactly one year from the date of the first observation. The only important changes were found in the right lower lobe, where the areas of density had enlarged and coalesced until the peripheral half of the lobe seemed to be consolidated. Only about one-third of the lungs remained ventilated.

Laboratory Findings: When first examined (October, 1923): Blood: Hemoglobin, 90 per cent; leucocytes, 7,150; polymorphonuclear neutrophiles, 66 per cent;

lymphocytes, 33 per cent; eosinophils, 1 per cent. The blood Wassermann was negative. Urinalysis was negative. Two sputum examinations were negative for tubercle bacilli; no cultures were made.

After return from sanatorium (July, 1924): Blood: Hemoglobin, 90 per cent; erythrocytes, 4,670,000; leucocytes, 10,200; polymorphonucelar neutrophils, 70 per cent; lymphocytes, 27 per cent; eosinophils, 3 per cent. Urinalysis was negative. The sputum was repeatedly cultured at this time for fungi and always *Monilia pulmonalis* Castellani was obtained in practically pure growth. Oval yeast-like cells with a few club-shaped segments were found every time in direct smears. These were Gram positive. An abundant smooth white growth developed on all the usual media. The same kind of oval cells were found in smears, and as the growth aged and assumed a "fluffy" appearance, bits of mycelium were found. Both continued to be Gram positive. Broth remained clear at first and then a thin pellicle formed. Acid and gas were negative on inulin, dulcite,

FIG. 6, Case 3, Mrs. J. H. T. (Nov., 1923). The areas of density in the right lung had increased in size and were becoming confluent. The density of the left lung had extended upward. Apices clear as before.

and lactose, but at first they were positive on maltose, glucose, and saccharose. There was no gas and very little acid on mannite. As subculturing was continued acid and gas were not produced in any of the sugars. Simultaneous examinations for tubercle bacilli were negative.

An autopsy was performed and cultures were made from the lungs about four hours after the body had been embalmed, but no growth was obtained.

Autopsy Findings: Examination was limited to the thorax and abdomen.

Lungs: The left lung was reduced to one-third normal size, and adhered closely to the chest wall, held by dense fibrous adhesions of firm consistency and difficult to tear. The visceral pleura in several places was more than 3 cm. in thickness and of the consistency of tough connective tissue. The delivered lung presented a ragged appearance, produced by tags of fibrous adhesions.

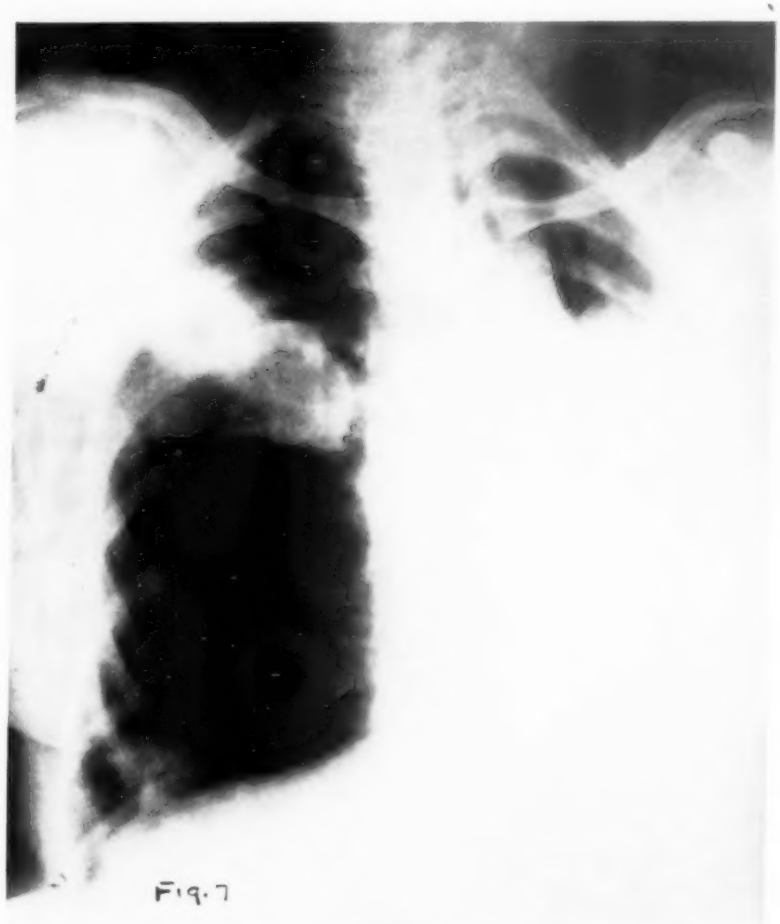

FIG. 7. Case 3. Mrs. J. H. T. (June, 1924). The mediastinum is displaced further to the left and only a small portion of the left upper lobe remains clear. The density in the right lung now extended from the periphery to the mediastinum, and some smaller areas had appeared at the right base. Both apices still clear. (For this roentgenogram we are indebted to Dr. C. P. Ambler, Asheville, N. C.)

The substance was quite resistant to cutting and its surface presented numerous small cavities rather uniformly distributed. The largest was about 4 cm. in diameter, and each connected with a bronchus. These gave the lung a cheese-like appearance. Most of these cavities were smoothly lined and many were filled with a clear jelly-like material. There was but little air-bearing tissue in either lobe. The large blood vessels were moderately thickened. The lymph-nodes were small, pigmented black, and only one contained lime salts.

The right lung was increased in size, was less firmly adherent to the chest wall than the left, and presented a pale mottled appearance. The visceral pleura was slightly thickened. Only parts of the upper and middle lobes were crepitant. On the cut surface a few cavities were found. These resembled closely those found in the left lung as to size, lining and contents, while

FIG. 8, Case 3. Mrs. J. H. T. (Oct., 1924). The areas of density in the right lower lobe had coalesced and now occupied the peripheral half of the lobe. Not much change in the left. The apices are still clear.

the remainder of the lung substance was consolidated as in pneumonia but differed in gross appearance. The consolidated portion was easily torn. The torn margins resembled frogs' eggs in shape and consistency. The entire cut surface presented a glistening, shiny, grayish, translucent appearance not unlike that of a colloid carcinoma. The entire right lung, except a portion of the middle lobe and the apex of the upper lobe, was consolidated. It was estimated that less than fifteen per cent of the lung was air-bearing.

Heart: The pericardial sac was drawn to the left by neighboring adhesions. The heart and vessels were otherwise normal in every respect. The aorta presented a few linear patchy areas of intimal thickening.

Liver: The liver was slightly enlarged and the cut surface had the appearance of passive congestion.

Spleen: The spleen was about normal in size and consistency. The cut surface presented several small firm tubercle-like bodies.

Other Organs: The other abdominal and pelvic organs were essentially normal.

Microscopical Findings were as follows:

Lungs: The bronchial epithelium was usually denuded—that which remained showed metaplasia. The bronchial walls were necrotic and infiltrated with mononuclear wandering cells and lymphocytes with an occasional red cell and polymorphonuclear leucocyte. This infiltration extended from the bronchial walls to the immediately surrounding alveoli. The remaining alveoli were characterized by the following changes: (1) The filling and dilatation of the entire alveolus with serum albumin. (2) The presence of a fibrin-like material occupying the alveolus with the exception of an area subjacent to the alveolar epithelium. Embedded in this fibrin-like material were peculiar large pale cells of different sizes and shapes, with unusually well defined cell membranes. There were definite connections between the fibrin-like material and the cell membranes. These cells were usually round, at times oval, but in the very large empty forms, pseudopodia-like structures occurred. The cytoplasm stained very pale, was reticular, granular or stippled, but occasionally crescentic-shaped forms occurred, formed by large clear empty spaces which crowded the nucleus and the cytoplasm to one end of the cell. The nuclei were leptochromatic but large and occupied about one-half of the cell space. Some cells contained two small nuclei. An occasional cell was found with pyknotic nucleus but without cytoplasm. (3) The occurrence of syncytial masses in the same alveolus with the fibrin-like material described above, but distinct and separate therefrom, usually lying at one end of the alveolus and but rarely in its center. They stained dark red and were large, round, kidney shaped or crescentic. In the smaller masses the nuclear structure was distinct and well defined while in the larger ones the nuclei were less well preserved and very poor in chromatin. The nuclei occurred in the center or the periphery of a mass.

The alveolar walls, especially about the larger bronchial vessels, were infiltrated with the same types of cells. Their vessels were engorged with red blood cells, but necrosis and rupture of their walls were also present. In some areas, compression atelectasis was prominent. The large pale cells previously described were to be found lining some of the alveoli, at times in aggregate nuclear masses. The lung tissue, subjacent to the pleura, was characterized by fibrosis, with an occasional small area of necrosis or infiltration with mononuclear wandering cells.

Lymph Glands: The lymph glands showed diminution in size of the cortical germinal centers and widening of the pulp medullary spaces with increase of the latter's contents.

We are indebted to Miss Florence M. Frost, formerly Director of Laboratories of the Polyclinic, for the careful cultural studies and for their description in this case. For performing the autopsy and for the description of the findings we are indebted to Dr. J. A. McIntosh, who was at the time Associate Professor of Pathology in the College of Medicine of the University of Tennessee. We desire also to express our appreciation to Dr. I. D. Michelson, emi-

nent mycologist and Professor of Bacteriology in the College of Medicine of the University of Tennessee, for the description of the microscopical findings, and for his invaluable assistance and helpful criticism in the preparation of this paper.

Discussion

In Case 1 the monilia infection apparently antedated the invasion of the tubercle bacilli. In Case 2 it is doubtful whether any direct relation existed between the moniliasis and the syphilis. Case 3 was apparently complicated by no concomitant factor, even though treated for many months as tuberculosis and preceded by influenza and pleurisy. It illustrates many of the salient features to be considered in dealing with fungus infection, emphasizing the importance of early recognition, of prompt differentiation, particularly from tuberculosis, and of repeated bacteriological and roentgen examinations. A unique feature in this case was the very sudden onset of the acute stage which continued unabated to a fatal termination in a relatively short time. In two cases of rather advanced tuberculosis, not mentioned in this series, we were able to demonstrate *Monilia pulmonalis* in the sputum, and in these cases we believe the yeast-like organisms were essentially secondary invaders.

It seems reasonable to assume that the monilia is a secondary invader, although it may be the chief factor in maintaining the chronicity of symptoms in some types of pulmonary disease. As Procházka,[7] Kotkis, Wachowiak and Fleisher,[9] and other writers have suggested, it is quite possible that some irritant agent, bacterial, toxic or mechanical, may initiate in the mucosa of the bronchus certain changes which make it possible for the monilia not only to maintain its existence but to grow. If these assumptions are correct, we may have to interpret bronchomoniliasis and probably many other types of bronchomycosis as conditions in which a primary factor, either still active or no longer acting, has initiated certain changes which have permitted the fungi to gain foothold and to find more or less permanent lodgment in the bronchi. The numerous cases, such as Case 3, in which a preceding bronchitis, influenza, pleurisy or pneumonia is mentioned, suggest a lowered resistance of the host, thus providing a suitable soil for the development of these fungi. We must concede that, once established, they are capable of becoming and not infrequently do become the essential and important element in maintaining the irritation in the lesions which they invade. In studying such cases, we should as a rule look beyond the relatively avirulent moniliae, without in any way ignoring the rôle of these fungi, for some other possible factor in the causation of the chronic inflammation. Also, we should certainly study very carefully all cases of chronic bronchitis, tuberculosis of the lungs, and other pulmonary diseases of long duration, especially those which in any way run a peculiar clinical course, and in such cases should insist upon repeated bacteriological examinations for fungi.

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Post-Vaccination Encephalitis*

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POST-VACCINATION encephalitis is a disease of unknown etiology that has appeared in recent years and which occurs without regard to the existence of known factors other than the presence of a recent vaccination against smallpox. The disease has a mortality rate of approximately 43 per cent and has associated with it pathological changes of the central nervous system which are similar to those found in the acute nervous manifestations occasionally noted following smallpox, chicken pox, measles and certain other acute infections.

History and Epidemiology

Lucksch[1] in June, 1924, published a series of three cases with post-vaccination nervous manifestations which occurred in Czechoslovakia. Following this publication, some 600 such cases have been reported from Europe—Holland, England, Germany and Norway, in the order named, having suffered the greatest number of cases. A number of additional European countries have had a few cases. Outside of Europe reported cases appear to be mainly confined to the United States. An isolated case or two has been reported from both Asia and Africa, while Australia, South America, Central America, Mexico and Canada have not reported instances of this complication, notwithstanding the fact that, during the last few years, authorities in these countries have been on the alert for them. In the United States 51 proven or probable cases have been recorded for the ten year period just prior to 1931. Forty-one of these occurred during the last three years of this period, or a rough estimate of one case for each 350,000 vaccine points sold in the United States during 1928, 1929, and 1930.

Not only has post-vaccination encephalitis, when judged on the basis of reported cases, shown a tendency toward unequal international distribution but within the various heavily involved countries it has shown a tendency to greater prevalence in certain localities than in others. This peculiar localization of cases seems scarcely to be explained by the relative number of vaccinations performed in the different localities or by differences in the methods of vaccination which were employed. Nor have the cases followed the employment of any particular vaccine virus. A striking number of instances have also been reported in

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which two cases have developed in the same family.

The heaviest incidence encountered in the United States occurred in a city of approximately 450,000 inhabitants, where among some 5,000 primary school vaccinations there were five cases, vaccinated within a period of thirteen days, which developed post-vaccination encephalitis. These cases were vaccinated by five different vaccinators who employed various types of single insertions. The same manufacturer's vaccine was used in each of the five cases. This fact, however, loses significance since this producer sold most of the vaccine virus used in the locality referred to during the fall of 1930. The same producer, moreover distributed vaccine virus to many localities of the United States without similar group incidence having been noted elsewhere. Moreover, cases are known to have followed the use elsewhere of vaccine prepared by several different manufacturers. In the affected areas of Europe cases have followed the use of rabbit brain virus, as well as calf strains from many sources including virus imported ready to use from countries in which post-vaccination encephalitis had not been reported.

The complication occurs usually but not invariably following the first or primary "take" and is, therefore, largely confined to children. Adults are, however, occasionally attacked. In affected countries where infant vaccination is practiced to a considerable extent a relative rarity of this complication has been noted following vaccinations performed during the first year of life, the incidence being estimated by Scott[5] as about one-sixth of that observed following primary vaccinations performed at later ages. However, if the comparison were made between primary vaccinations under one year and those performed at school age the figure would be probably even more favorable to infant vaccination. In the United States the cases so far reported range from 3 to 49 years in age. Both males and females are susceptible. The complication may develop from a few days to several weeks following the vaccination but there is a striking tendency for it to make its appearance from the tenth to thirteenth day inclusive following primary vaccinations, with a tendency for the interval to be somewhat shortened in cases which follow secondary vaccinations. In other words post-vaccination encephalitis when it develops usually appears when the vaccination is at its height.

European cases have usually followed multiple insertion vaccinations, this, until recently, being the approved method of vaccination in the affected countries. In some instances the complication has followed local "takes" of exceptional severity and in at least one instance was accompanied by a synchronously appearing generalized eruption interpreted as generalized vaccinia.

European cases have, however, appeared following single insertion vaccinations and in the United States all the cases have followed this type of insertion. The evidence, moreover, is clear that in many instances the local "takes" ran a satisfactory course and

were not of exceptional severity.

Clinical Picture

The onset in post-vaccination encephalitis is usually sudden with a feeling of illness, fever, vomiting and headache. Drowsiness and coma may supervene rapidly.

The neurological symptoms vary markedly in individual cases and may point to a major involvement of the meninges, the brain, the brain stem or the cord. Depending upon the regions involved several types of the disease have been recognized by those who have studied particularly the clinical manifestations.

1. *Meningeal Type.* This type is common in infant cases, is marked by vomiting, headache, rigidity and retraction of the neck and often by convulsions. The Kernig and Brudzinski signs may be positive and a meningitic cry may be present.

2. *The Cortical Type.* In this type convulsions are the most prominent symptom. In two cases of our series convulsions appeared suddenly after the children who were considered to be quite well had been put to bed for the night. Both tonic and clonic convulsions may occur in the same individual accompanied by loss of consciousness. Disturbances of sight and hearing may be present. Such attacks may be rapidly fatal, death in one of the cases investigated resulted within twenty-four hours from the onset of symptoms which made their appearance eight days following the vaccination. In one non-fatal case of this type there is marked mental deterioration with attacks of petit mal apparent after a period of two years. In another case attacks of petit mal are still appearing six months after the subsidence of acute symptoms.

3. *Brain Stem Type.* In this type somnolence, rigidity, tremors, twitching, with altered reflexes, are usual features. The eye muscles usually escape but may show involvement in some cases.

4. *The Myelitic Form.* Here the involvement of the lower motor tracts may produce a picture simulating that of poliomyelitis with crippling of one or more extremities. However, cases showing a complete paralysis of the lower limbs, such as would almost surely give a bad prognosis for prompt recovery of function in poliomyelitis, may clear up dramatically within a few days. In other instances the myelitic form may present the picture of a transverse myelitis with loss of motion and sensation below the involved segments. In one case of this type which we have observed there is still complete loss of motion and of sensation below the affected segment after a period of six months. Cases of this type have, however, been reported in which recovery has taken place more or less promptly.

5. *Tetanic Form.* A tetanic type with trismus and opisthotonus as prominent symptoms has been occasionally noted both in this country and in Europe. Such cases are of especial interest in that they may be confused with post-vaccination tetanus. The clinical picture in these cases, however, has as a rule been rather atypical for tetanus.

While these five clinical types of post-vaccination encephalitis have been recognized among pathologically confirmed cases and are of assistance in

the clinical understanding of the disease, it should be remembered that the classification is an arbitrary one and that most cases present symptoms suggesting two or more of these clinical groups. For instance, headache, drowsiness or coma, rigidity of the neck, convulsions—often of Jacksonian type, incontinence or retention of urine, altered reflexes and paresis or paralysis are features which may be met in cases which differ markedly in other respects. Sensory disturbances have been most frequently noted in the lower extremities. Loss of hearing and sight have been noted in a few instances. It is to be noted that alertness is sometimes encountered in place of the usual lethargy and pains may be prominent symptoms. Trophic disturbances have been occasionally met with.

Differential Diagnosis

Cases have been mistaken for meningitis of epidemic or tuberculous type, meningismus, encephalitis lethargica, poliomyelitis, sunstroke, cerebral hemorrhage, tetanus, epilepsy, and hysteria. In central nervous disorders the patient should always be examined for the presence of a recent vaccination "take". The presence of a vaccination performed within 30 days of the onset of nervous symptoms should suggest the possibility of post-vaccination encephalitis. In case the onset falls between the tenth and thirteenth days inclusive, this fact is of equal, if not indeed of greater importance, in making a diagnosis of post-vaccination encephalitis than is the character of the nervous symptoms. Furthermore, when the differential diagnosis lies between post-vaccination encephalitis and post-vaccination tetanus an interval of 14 days or less from vaccination to onset of symptoms strongly favors post-vaccination encephalitis, while one of 17 to 24 days or longer strongly favors post-vaccination tetanus. The spinal fluid in post-vaccination encephalitis is clear, shows no visible or cultivatable organisms, and may be essentially normal. However, it is usually under increased pressure with an augmented cell count. In a few instances vaccine virus has been demonstrated in the cerebro-spinal fluid but this has been an exceptional finding.

Pathology

The central nervous system changes encountered in post-vaccination encephalitis are distinct from those of poliomyelitis or of encephalitis lethargica, but are similar to those encountered in the nervous system involvement which occasionally follows acute infections other than vaccinia. The characteristic finding in these cases consists of adventitial and periadventitial round cell infiltration mainly confined to, but distributed throughout the white matter of the brain and cord. With the Weigert or other appropriate staining method zones of myelin degeneration may be seen centered about the smaller vessels and gradually fading into normal myelin tissue. These perivascular lesions usually, though not always, have shown a symmetrical distribution. Their number and intensity may, however, vary at different levels, a fact which accounts for the variability of symptoms.

Prognosis

Among the cases so far reported 43 from each hundred have ended

fatally. In non-fatal cases the recovery is usually prompt and without sequelae. Exceptions to this rule are, however, far from rare.

Prevention

Beyond the fact that vaccinations performed during the first year of life are relatively less liable to be followed by post-vaccination encephalitis than are primary vaccinations performed later, little is known as to prevention.

The Rolleston Commission in Great Britain recommends the abandonment of multiple insertions in favor of a single small implantation of virus and is experimenting with dilutions of lymph. While such measures aimed toward a milder type of local and general vaccination response would seem to be indicated, their value in the prevention of the complication under discussion has yet to be established.

Treatment

In addition to symptomatic treatment great care should be taken to prevent the development of bed sores, or of cystitis in cases requiring catheterization. Horder,[3] Hekman,[2] and Grüneberg[1] have utilized the serum from vaccinated individuals, preferably those recently vaccinated, in the treatment of fourteen cases of post-vaccinal encephalitis and consider their results as encouraging. The same treatment has been employed in a few cases in this country but without any clear indication as to its value.

Etiology

While a definite relationship between vaccinia and the occurrence of post-vaccination encephalitis has been established, the exact nature of this connection is still obscure. Attempts to produce the condition in laboratory animals have in the opinion of most workers met with uniform failure. Various hypotheses have been advanced in an effort to explain the occurrence of the condition but time will not permit of their consideration.

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Clinical Aspects of Portal Cirrhosis*†

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STUDIES on the experimental pathology of the liver have thrown light on many obscure clinical features of portal cirrhosis, and have shown the significance of certain points concerning the genesis and course of the disease which are not generally appreciated. The fact that ascites can be produced only occasionally in animals, and then only with difficulty, and after much injury has been done to the liver, suggests that in man the clinical syndrome of portal cirrhosis with ascites must represent the terminal stage of a long-lasting disease. Just as the general well-being of animals which are receiving daily sublethal doses of hepatic poisons persists until the amount of functioning hepatic tissue is reduced to a critical point, so does the human victim of cirrhosis frequently remain unaware of the presence of the disease until irreparable injury has been done.

The hepatic lesions which are included under the generic term of hepatic cirrhosis are supposed to represent the end-result of a process of repair and progressive fibrosis consequent on successive focal degeneration or necrosis of the hepatic cells at the periphery of the lobules.[1,2] The reparative processes eventually restrict the portal, venous and capillary bed, and the anatomic end-result is disorganization of hepatic structure with lobulation and formation of adenomas. The physiologic end-results are two: portal hypertension and hepatic insufficiency.

Theoretically any toxic substance which is capable of destroying or injuring hepatic cells, and which may act intermittently over a long period of time, is capable of producing the anatomic lesions of cirrhosis. Whereas a number of factors probably enter into the production of the disease, the end-result is apparently not specific for any particular agent. So far as can be seen now, it appears that the various forms of cirrhosis resulting from diffuse infectious processes such as syphilis, the use of alcohol, or of several other chemical poisons, are much alike clinically and even pathologically. It is for this reason that a clinical classification of cirrhosis is so hard to make. Many clinical types have been described, some of which are reasonably well defined. Among these may be mentioned: (1) portal cirrhosis with either hypertrophy or atrophy of the liver; (2) biliary cirrhosis, either primary or secondary to extrahepatic biliary obstruction; (3)

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pigmentary cirrhosis (hemochromatosis); (4) capsular cirrhosis (polyserositis), and (5) the cirrhosis of Wilson's disease. For the purposes of this paper portal cirrhosis may be defined as the end-stage of a degenerative or inflammatory hepatic lesion which has reached the stage of lobulation and which more or less restricts the portal venous circulation.

Etiology

Experimental cirrhosis has been produced chiefly by toxic substances which enter the liver through the portal blood stream. Biliary cirrhosis secondary to experimental obstruction of the common bile duct may progress to portal obstruction and ascites. Clinically, a similar situation prevails. There are many etiologic agents which are supposed to be capable of causing hepatic injury, but the evidence against most of them is largely circumstantial. Alcohol may be cited as a case in point. Although about fifty per cent of patients with portal cirrhosis admit the use of alcohol, not all of them have been heavy drinkers, and in only about five per cent of patients who exhibit marked evidence of alcoholism do hepatic lesions of any great consequence develop. There is, however, as Rowntree[41] and others[43] have shown, some parallelism between the death rate from alcohol and that from hepatic cirrhosis. Functional hepatic injury after abuse of alcohol has been demonstrated by v. Bergmann,[4] by means of tests on the rate of excretion of bilirubin; he has shown, also, that a similar delay in excretion of bilirubin exists in chronic alcoholism and in portal cirrhosis.

Although alcohol will not produce entirely satisfactory experimental cirrhosis, hepatic necrosis and fibrosis may follow its prolonged administration.[15] It seems well established that it is capable of producing structural hepatic injury, but whether it acts directly or through some intermediary product is unknown. It is known to produce changes in the gastro-intestinal tract which may in themselves be the source of toxic substances, or it may permit absorption of the latter from the intestine. It is also recognized that alcohol may act as a solvent for toxic organic substances of intestinal origin. Obviously not all cirrhosis is of alcoholic origin. In India, alcoholism is rare but cirrhosis is common.[48] Yang,[52] in reporting eighty-four cases of cirrhosis in Chinese, found that alcohol could be a factor in only two cases.

The relation between cirrhosis and syphilis is also debatable. The typical result of syphilitic inflammation in the liver is the so-called hepar lobatum, but diffuse syphilitic hepatitis may produce a cirrhotic process indistinguishable from the alcoholic type.[37] LeDuc[27] claimed that seventy-five per cent of patients with cirrhosis have microscopic evidence of syphilis elsewhere in the body. Experience at The Mayo Clinic has shown that one-fourth of the patients in the ascitic stage of cirrhosis have had either a positive Wassermann reaction or a more or less definite history of syphilis. Of nine of the patients who came to necropsy with cirrhosis and serologic evidence of syphilis, only one had typical hepar lobatum; the remainder presented the usual picture of

atrophic cirrhosis. I have therefore included in this study cases of portal cirrhosis in which syphilis may have been a cause, but in which the symptoms did not disappear under specific treatment.

In my experience, cholecystitis and infection of the biliary tract are frequently associated with cirrhosis, but the evidence is not sufficiently complete to differentiate cause and effect. Koster[26] and his associates have described early fibrotic changes in the periportal tissues of patients with chronic cholecystitis, and expressed the belief that these changes were secondary to cholecystic disease, and that the spread of infection was by way of lymphatic channels. Other types of gastro-intestinal disease may enter into the genesis of cirrhosis. As Opie[39] has suggested, a combination of bacterial infection and chemical intoxication may be involved. The liver may also be injured more or less severely by many of the infectious diseases. In Yang's[52] series, fifty patients gave histories of bacillary dysentery or typhoid fever; a previous history of typhoid fever is not uncommon in cases of cirrhosis studied at The Mayo Clinic. Other possible etiologic factors are inorganic arsenical poisoning,[38] hyperthyroidism, toxemia of pregnancy, chronic intoxication[39] from protein and malaria.

Certain observations on the experimental aspects of cirrhosis must be considered in a study of the etiology of the condition in man. Research workers agree that when they stop giving the drug which is destructive to the liver, the liver of the animal returns to an approximately normal state provided the lesion is not too far advanced. From this one must infer that in man the poisons which produce cirrhosis must operate continuously over a long period of time. Experimentally there is also marked individual variation in the response of the liver to chemical injury. As Bollman and Mann[8] have suggested, the response may be due to the state of the liver at the time the toxic agent acts, or it may bear some relationship to the hepatic reserve of glycogen present in the organ at the time.

An obscure point in the pathogenesis of cirrhosis is the nature of the overgrowth of connective tissue which follows some forms of hepatic injury, and which is absent in others. The stimulus to formation of connective tissue apparently must be an essential element in the etiology of portal cirrhosis. It is also recognized that previous hepatic injury leaves the liver with a variable amount of regenerated hepatic tissue, which has been shown to be unusually susceptible to injury. In other words, successive degenerative lesions of the hepatic parenchyma are more and more easily produced, and each in turn interferes further with the hepatic blood supply. The ability of experimentally produced anoxemia[21,41] to cause degenerative changes in the hepatic cells must also be considered. Recent studies by Rich[41] show that anoxemia may operate as a cause of depressed hepatic function; from these studies it is apparent that the hepatic arterial blood flow may be of great importance in determining the course and progression of any hepatic lesion.

Clinical Stages of Cirrhosis

It is clearly established that, in both animals and man, portal cirrhosis may be present without ascites or, in fact, without any marked symptoms of visceral disease. This may be attributed to the enormous physiologic reserve of the liver, to its remarkable regenerative properties, and to the collateral circulation which accompanies the sclerosing types of hepatic lesions. The course of cirrhosis may therefore be divided into two stages, one a preascitic stage, and the other an ascitic stage; or, as Rowntree[9] has stated, an hepatic lesion may exist either with a compensated or a decompensated portal circulation. The relative frequency of the two stages of the disease is not definitely known, but it has been said that ascites develops in from fifty to eighty-five per cent of cases of cirrhosis. The compensated, or preascitic, stage of the disease has attracted little attention; the attention of physicians has remained focused on the end-stage of the disease. More complete knowledge of the nature and duration of the preascitic stage is now highly desirable. I have, therefore, attempted to review the cases of portal cirrhosis seen at The Mayo Clinic from 1924 to 1929 inclusive with the idea of learning something about the clinical course, the symptoms of the earlier stages, the criteria on which a prognosis can be based, and the rationale of medical and surgical treatment.

The material to be studied comprises 399 cases divided into three groups: (1) 135 cases in which nodular cirrhosis of the liver was discovered in the course of surgical operations for other abdominal lesions; (2) 152 cases in which a clinical diagnosis of portal cirrhosis in the preascitic stage was made, and (3) 112 cases of cirrhosis in the terminal or ascitic stage. Some idea of the incidence of cirrhosis among patients in the clinic may be gained from the fact that, in the period of six years covered by this study, 399 patients were found to have the disease in a total of approximately 400,000.

Cirrhosis Discovered at Operation. In the group of 135 cases, in which the disease was discovered at operation, hepatic lesions were suspected in only a few, and then because the spleen had been found to be enlarged. I have excluded from this group patients with obstructive lesions of the common bile duct, and those whose hepatic lesions were more localized than diffuse. In some of this group biopsy of the liver was obtained, but in most instances the diagnosis was made from the gross appearance of the liver only. It is probable that some cases were overlooked, since the liver may appear grossly normal and yet contain the microscopic lesions of portal cirrhosis. It is also probable that there were some positive errors of diagnosis, but in general the surgeon's opinion may be regarded as reliable.

The observations at operations in which cirrhosis was found accidentally are given in figure 1. The number of cirrhotic livers discovered at operation on the gallbladder is not large, considering that approximately 7,000 operations were done on the biliary tract in this period. The discovery of cirrhosis at this type of operation may perhaps be explained on the basis of the proximity of the liver and the

extrahepatic biliary tracts. However, many experienced surgeons feel that lesions of the gallbladder, of long standing, may lead to a cirrhotic process in the liver; at least it is agreed that the two conditions are not infrequently associated. This view, which rests on clinical impressions only, is partially substantiated by the views of Koster[26] and his collaborators. There is, of course, a possibility that the disease of the liver may have been primary, and that of the gallbladder, secondary.

That cirrhosis was found in the course of approximately twenty operations which were done for peptic ulcer was somewhat surprising. It may be that these ulcers were secondary to the hepatic lesion present, since Bollman[7] has found that in experimental obstructive jaundice, typical callous ulcers of the duodenum are commonly found. Berg and Jobling[3] have also advanced the view that hepatic lesions may favor the formation of peptic ulcers.

The cirrhosis which accompanies Banti's disease needs no further comment. Johnston's[23] recent paper contains a summary of the current views on the subject. Thirteen of the patients with Banti's splenomegaly had cirrhosis of marked degree, with reduction of about fifty per cent in the size of the liver. Hepatic functional tests were made in a number of these cases and only moderate retention encountered. Excluding the group with Banti's disease, only eight of the 135 patients had definite splenic enlargement, and in only a few was there any mention of the collateral circulation. From this fact it would appear that in primary portal cirrhosis an enlarged spleen occurs late, when the portal circulation is greatly restricted, and that interference with flow of

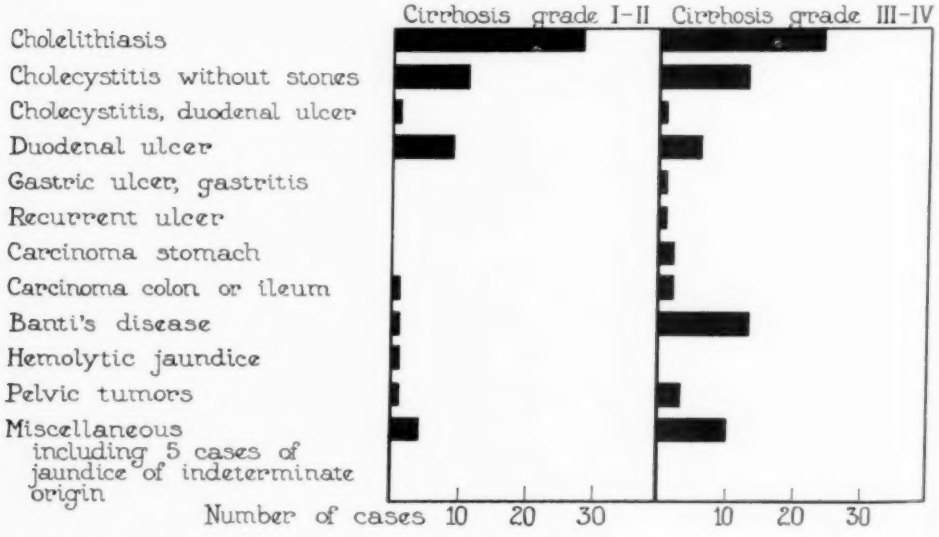

FIG. 1. Conditions found at operation in cases in which operation disclosed cirrhosis.

portal blood must exist for some time before collateral channels are established.

The symptoms which brought these patients to operation are of some interest. Thirty had typical gallbladder colic; twenty-eight had pain in the upper part of the abdomen, and soreness associated with some indigestion; eighteen complained of poorly localized or bizarre abdominal pain; seventeen had the typical syndrome of peptic ulcer, and ten of these seventeen gave histories of hematemesis and melena. Gastro-intestinal bleeding, without other symptoms, was noted in nine cases. Nine patients gave histories of jaundice. In reviewing these histories, it is difficult to see how hepatic disease could have been suspected in more than a small percentage of the cases. The routine inquiries as to alcoholism and syphilis gave little, if any, information of value since only nine of the patients admitted the abuse of alcohol and only six gave histories of syphilis.

The outcome of the disease in this group of cases is of considerable interest. Nine patients subsequently had ascites; twenty-four have died, and in at least fourteen the hepatic lesion found at operation apparently was responsible for death. The immediate surgical mortality in the 135 cases was not high, so that the subsequent death of the patients may perhaps be attributed to the progress of the disease in the liver. Of the patients with Banti's disease only two have died, and the death of one could not be attributed to hepatic disease.

Many of the surviving patients have written to complain of indefinite gaseous dyspepsia, weakness, or gastro-intestinal bleeding. On the other hand, a large group have replied to letters of inquiry with the statement that they were perfectly well. The subsequent health of a number of the patients with livers described by the surgeon as being markedly atrophic or "hobnail" in appearance, has remained good and they have experienced no inconvenience. In many of these cases it is hard to see how the operation could have had any effect on the course of the cirrhotic process, but in some the formation of postoperative adhesions may have helped to establish collateral circulation, which in turn may have deferred the development of ascites. In some the removal of diseased gallbladders may have had beneficial effect.

Preascitic Portal Cirrhosis Diagnosed Clinically. In the group of 152 cases in which a clinical diagnosis of portal cirrhosis was made in the preascitic stage, confirmation was not obtained by operation or necropsy. A large percentage of these diagnoses were made because a history of alcoholism or syphilis was associated with the finding of a large liver or spleen and definite retention of dye. The accuracy of diagnosis may, of course, be questioned, and no doubt some of the patients were suffering from carcinoma or other serious visceral disease. Diagnostic accuracy in the early stages of cirrhosis is disappointingly low and positive criteria have not as yet been established. Often the few symptoms that present themselves are not pathognomonic, and the diagnosis must frequently rest on objective evidence.

In the series of 152 cases the most common complaints were of vague abdominal pain, gaseous indigestion, weakness, and intermittent jaundice, which was usually painless or almost painless. An enlarged, firm liver was noted in the majority of the cases, and a palpable spleen was commonly found. Edema and signs of collateral circulation were uncommon. In this stage of the disease there was usually only moderate retention (graded 1 or 2) of phenoltetrachlorphthalein or bromsulphalein. More delicate functional tests[1,19] might have revealed more striking changes.

Seventy-two of the 152 patients are known to be dead; fifty-eight cannot be traced, and only fourteen are known definitely to be living after periods of observation averaging about four years in length. A follow-up study of this group is now being carried out, so that the details presented here are necessarily incomplete. Ascites is known to have developed in nine of the cases. A few other patients who had a small amount of fluid at the time of examination appear to have recovered completely. One patient in whose case the diagnosis of syphilitic hepatitis was considered, but not proved, regained health under the use of iodides. Another patient with a large liver and marked retention of dye was reported as being well a year after examination. Two patients appear to have died suddenly from gastro-intestinal hemorrhage, and several have died in coma. The high mortality in the group gives startling evidence of the gravity of the situation even in the early stages of cirrhosis.

On the basis of experimental evidence, it seems probable that in the earlier stages of cirrhosis the liver should be able to regenerate, and to become fairly normal, provided the cause of the disease could be recognized and removed. That this actually happens at times is shown by the cases, which are not infrequently reported, in which a man who has been a heavy drinker, and who has begun to show signs of cirrhosis, stops drinking, gets well, and stays well. When etiologic agents continue to act, however, as they apparently do in a majority of cases, the pathologic process continues unchecked, and a fatal termination is the rule.

Cirrhosis with Ascites. The appearance of free fluid in the abdomen, which has been characterized as indicative of decompensation of the portal circulation, appears to mark a critical point in the course of the disease. All of the 112 patients of this group had ascites already at the time of registration at the clinic and presented typical examples of the ascitic stage of portal cirrhosis. From all of the cases in the group other causes of ascites could be definitely excluded; in addition, the diagnosis was confirmed in half of the cases by surgical exploration or necropsy. Eighty-two of the patients were males and forty were females; sixty per cent were between the ages of forty and sixty years.

A careful inquiry was made into the early symptoms noted in each case, and the results are presented in figure 2. It is significant that approximately sixty per cent of the patients had suffered from various gastro-intestinal symptoms for from two weeks

to twenty years prior to the development of ascites. The average duration of these symptoms was considerably more than a year. Loss of strength was common, but loss of weight does not seem to have been conspicuous until shortly before the appearance of ascites. As in the group without ascites about a fourth of the patients gave histories of slight, intermittent, painless jaundice, often associated with diarrhea, vomiting, and abdominal cramps. Hematemesis was noted as an early symptom in less than ten per cent of cases. Ascites developed suddenly in about eighteen per cent. In six cases, an enlarged liver or spleen had been found, or a definite surgical diagnosis of cirrhosis had been made from two to ten years before the development of ascites.

The early symptoms were in contrast to those which were complained of at the time the patient registered at the clinic. After the appearance of ascites, loss of strength and weight were much more striking, and abdominal pain or distress was complained of by about half of the patients. Jaundice was present in thirty-eight instances. Gastro-intestinal bleeding was twice as common as in the early stages of the disease.

The physical evidences of the decompensated stage of hepatic cirrhosis are too well known to require particular comment. The combination of characteristic "hepatic" facies, slight jaundice, ascites, edema, and visible collateral circulation, constitutes a picture familiar to all clinicians. Certain incidental features are not so well known. Forty-seven of the patients with ascites had one or more hernias; five had two, and one patient had three. This high incidence is surprising when one considers that in other types of ascites or abdominal enlargement hernia is less frequently encountered.

About fifty per cent of the 112 patients of this subgroup had more or

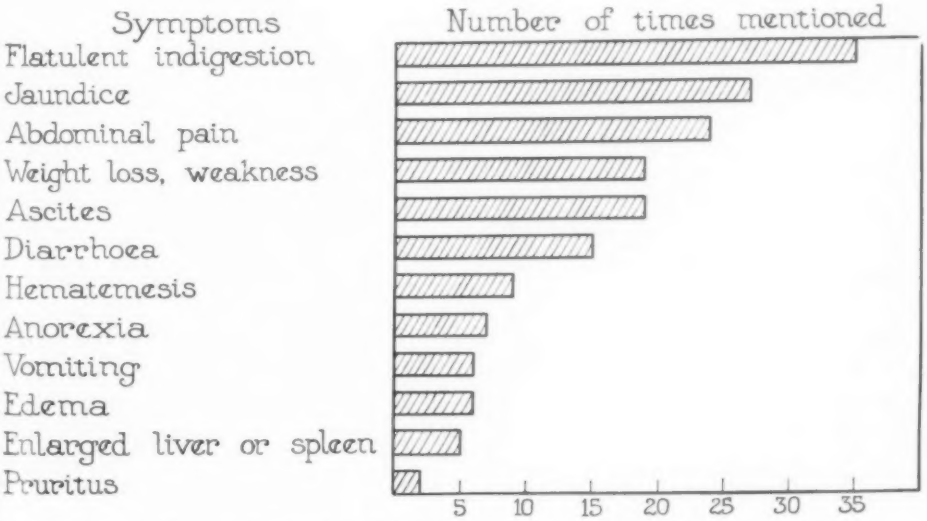

FIG. 2. Early symptoms of portal cirrhosis in cases in which ascites developed.

less marked collateral venous circulation over the abdomen, lower part of the thorax, or lumbar region. In one case, the size of the peri-umbilical veins was striking; in another, a very large vein was noted over the thorax, and appeared to terminate in the axilla (figure 3).

A palpable liver was noted in sixty per cent of the 112 cases. The degree of enlargement varied greatly at different times in individual cases, and in some cases the size appeared to decrease while the patient was under observation. The spleen was palpable in about forty per cent of the cases. From a consideration of data obtained at operation and at necropsy in this group, however, it would appear that clinical conceptions of the size of the liver and spleen may not be accurate, particularly when ascites is present.

Laboratory Tests

The laboratory studies require only brief mention. What is to be said about them applies to the series of 112 cases with ascites. Scanty and highly concentrated urine was the rule. Examination of the urine for urobilin and urobilinogen gave variable results which seemed to depend on the presence or absence of slight jaundice. About twenty-five per cent of the patients had slightly elevated values for serum bilirubin at some time while they were under observation. Deep jaundice, however, was rare. In ten cases, the bile acids in the serum were determined by the method of Aldrich,[17] and in all normal values were found.

In about forty per cent of the cases there was a definite anemia, with hemoglobin of fifty per cent or less. The characteristics of the blood in general corresponded to those previously described by King[24]. The values for blood sugar and blood urea were normal in practically all cases, although in fifteen of the group the concentration of urea in the blood was elevated at some time in the course of treatment. In one case, and on one occasion only, a very low value for

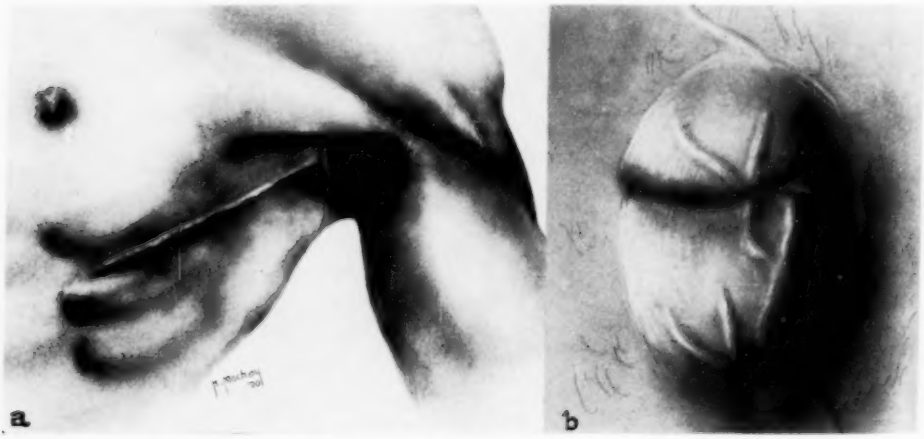

Fig. 3. Unusual types of collateral circulation in portal cirrhosis: *a*, in the axilla; *b*, about the umbilicus.

blood urea (4 mg. in each 100 c.c.) was encountered. In two cases postoperative hypoglycemia was noted. Following the appearance of papers by Minot and Cutler,[34] and Ellsworth,[11] determinations of guanidine in the blood were made in a number of cases, but striking or significant changes were not noted.

The tests of hepatic function with bromsulphalein or phenoltetrachlorphthalein proved their dependability in this series of cases, as in other series of cases reported from the clinic.[18] These tests were done in eighty-seven cases, and in eighty, positive results were obtained. The results of repeated tests of hepatic function were remarkably constant in any given case, providing jaundice was not present. In exceptional instances there was reduction in the degree of retention of dye as the patient improved. This was particularly true when the original cause of hepatic injury was discovered and effectively treated.

Tests of hepatic function by means of dyes appear to be influenced by three factors: (1) the amount of blood coming to the liver through the portal vein and the hepatic artery, (2) the presence or absence of jaundice, and (3) the amount of functioning hepatic tissue. The degree of retention of dye seems to indicate, in a general way, the degree of parenchymal injury, although clinically the degree of retention of dye could not be correlated with the size of the liver, the degree of ascites, or the degree of toxemia presented by the patient. The prognostic value of the test, however, appears to be considerable, since patients with retention of dye, graded three or four, on the average, pursue a much less favorable course than those with low degrees of retention.

Cause of Symptoms of Portal Cirrhosis with Ascites

It seems advisable to review briefly what is known of the serious symptoms and signs of portal cirrhosis in the ascitic stage. Pain may be of enteric origin, although other causes cannot be eliminated.[28] Jaundice is apparently an expression of hepatic parenchymal degeneration. Hemorrhage appears to be due most frequently to leakage from esophageal varices. These appear to be present in every case of cirrhosis, although they are not always demonstrable at necropsy, since special injection technic may be required to disclose them. In life they have been demonstrated rarely, since esophagoscopy has been performed only infrequently in this group of cases. Gilbert[16] and his associates have performed this procedure in twelve cases, and have found dilated esophageal veins in all. Wolf[51] has demonstrated eosphageal varices by roentgenologic methods in two cases, and Kirklin and Moersch[28] are reporting a case in which such varices were demonstrated by roentgenologic methods and by esophagoscopy.

The factors which favor bleeding from these varices are not known. Physical exertion seems to precipitate the hemorrhage in some cases. In others, the hasty eating of coarse foods apparently has provoked hemorrhage. A number of patients bled after paracentesis and after operation. Many other patients stated that their

bleeding had begun when they were asleep, a fact that may be explained on the basis of venous stasis and congestion. It is, of course, generally recognized that a hemorrhagic tendency of unknown nature and variable severity exists in hepatic disease of all types, and it is certainly a common accompaniment of portal cirrhosis, although laboratory studies on the coagulating properties of blood in this disease may not always give conclusive proof of the hemorrhagic tendency.

The cause of the ascites has been debated since time immemorial, and a great many possible explanations have been brought forward. Portal obstruction alone is not sufficient, and other factors must be involved. Herrick[29] has expressed the belief that ascites appears when vascular injury has reached such a point that the pressure in the hepatic artery can affect that in the portal system. Feissinger[12] has attributed it to acute degenerative changes and swelling of the hepatic cells, and secondary occlusion of the portal capillaries which are confined in an inelastic framework. Bollman[6] has demonstrated the effect of dietary factors which could hardly operate except through their effect on the hepatic cell or by peritoneal irritation. Occasionally ascites will develop from portal thrombosis. Mann[30] has expressed the belief that four factors are involved: (1) interference with portal circulation, (2) lack of absorption from the peritoneal surfaces and from the intestines, (3) peritoneal irritation, and (4) reduction in the amount of functioning hepatic tissue. It has also been suggested that toxic substances produced by degenerating hepatic cells may interfere with the renal elimination of water.

Little, if anything, is known about the nature of the so-called hepatic coma which is so frequently a terminal event in portal cirrhosis. It is generally agreed that the chemistry of the blood is not altered as it is in the hepatectomized animal, although in occasional cases there is hypoglycemia. Failure of the detoxifying function of the liver has been regarded as significant. Becher[2] has noted an increase in the amount of phenol and phenol derivatives in the blood of patients with cirrhosis of the liver, which he has attributed to failure of this function.

Prognosis

The prognosis of portal cirrhosis is grave in any stage of the disease. As was previously noted, the mortality in the preascitic stage is high, even in cases in which the disease is discovered accidentally at operation. Of the 112 patients in the group with ascites, eighty-four have died. Coma, gastrointestinal hemorrhages, and intercurrent diseases were the principal predisposing causes of death. Six patients died after operations, and the death of four of them was directly attributable to hemorrhage. Twenty-seven patients died at home from causes unknown to the clinic. The average duration of life of the patients was about sixteen months after the appearance of ascites. The twenty-eight patients who are living have survived, on an average, about thirty-eight months after the development of ascites. These figures, although not encouraging, are better than those

previously given in the older literature, a point which is demonstrated in figure 4. Formerly the average duration of life after the development of ascites was from two to five months. The longer period of survival of the patients in the group considered in this paper may possibly be attributed to recent improvements in the medical treatment of cirrhosis, but such factors as earlier diagnosis and treatment, a lower incidence of marked alcoholism, and a high degree of intelligent coöperation on the part of many of the patients must also be taken into account. The prognosis is obviously better in the occasional case in which the causes can be found and eradicated.

The prognosis in individual cases can be determined roughly by four factors: (1) the degree of retention of dye, (2) the response to treatment with diuretics, (3) the general state of nutrition of the patient, and (4) the presence or absence of complicating disease. Patients with low degrees of retention of dye, who respond favorably to administration of diuretics, appear to do particularly well. The same may be said of patients who remain in good nutrition and who are willing to make the necessary adjustments in their manner of living. Complicating diseases, particularly those of an infectious nature, appear to add greatly to the gravity of the situation.

Observations at Necropsy

The pathologic changes seen in cases in which patients have died with portal cirrhosis have been described

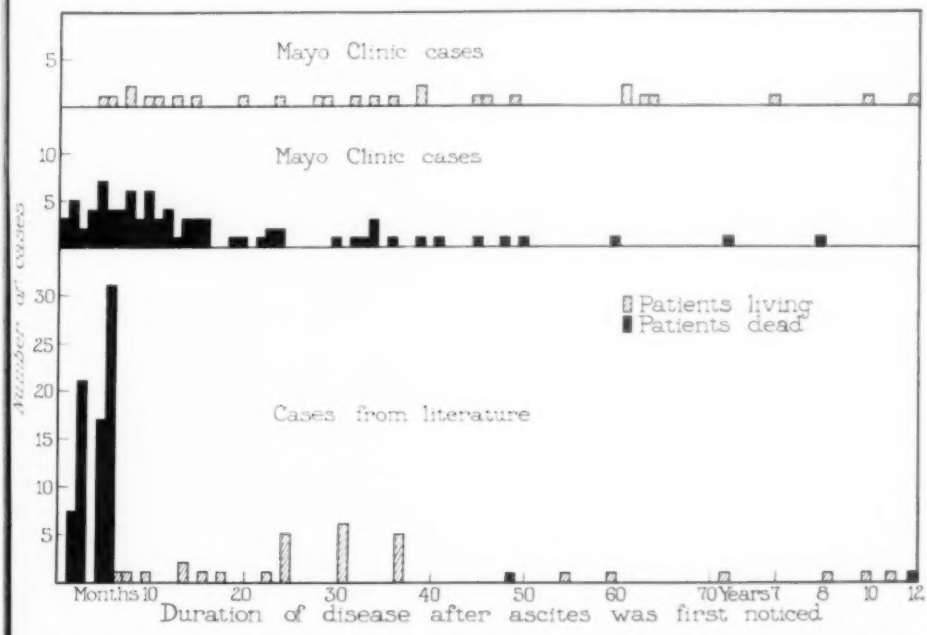
Mayo Clinic cases
Mayo Clinic cases
Patients living
Patients dead
Cases from literature
Number of cases
Months 10 20 30 40 50 60 70 Years 7 8 10 12
Duration of disease after ascites was first noticed

Fig. 4. Average duration of life in portal cirrhosis with ascites: upper two lines, cases seen at The Mayo Clinic, 1924 to 1929 inclusive; lowest line, cases noted in the literature prior to 1921.

often. For the sake of completeness, I include here the significant features disclosed in a group of recent postmortem examinations made at the clinic, in the course of the years 1924 to 1930 inclusive. A decrease in the size and weight of the liver is fairly uniform in this series, as may be noted in figure 5. The size of the liver does not seem to bear any relationship to the weight of the spleen or to other changes found at necropsy. In Nissen's[36] series, reported ten years ago, the average life of the patients was shorter, and the average weight of the liver was considerably higher.

Collateral circulation was demonstrable in practically all cases. In several, the omentum was adherent to the abdominal wall, and represented spontaneous omentopexy. Esophageal varices were present in every instance, and in at least one-third of the cases there was evidence of recent bleeding into the gastro-intestinal tract. In three cases intraperitoneal hemorrhage was noted. Edema at various points of the gastro-intestinal tract was common, often associated with congestion and small regions of superficial ulceration. Chronic gastric or duodenal ulcers, either healed or active, were present in about twenty per cent of cases. Fibrosis of the pancreas was noted in more than one-third of the group. Cholelithiasis was found in five cases; chronic cholecystitis without stones was noted in twelve, and marked edema of the gallbladder in two.

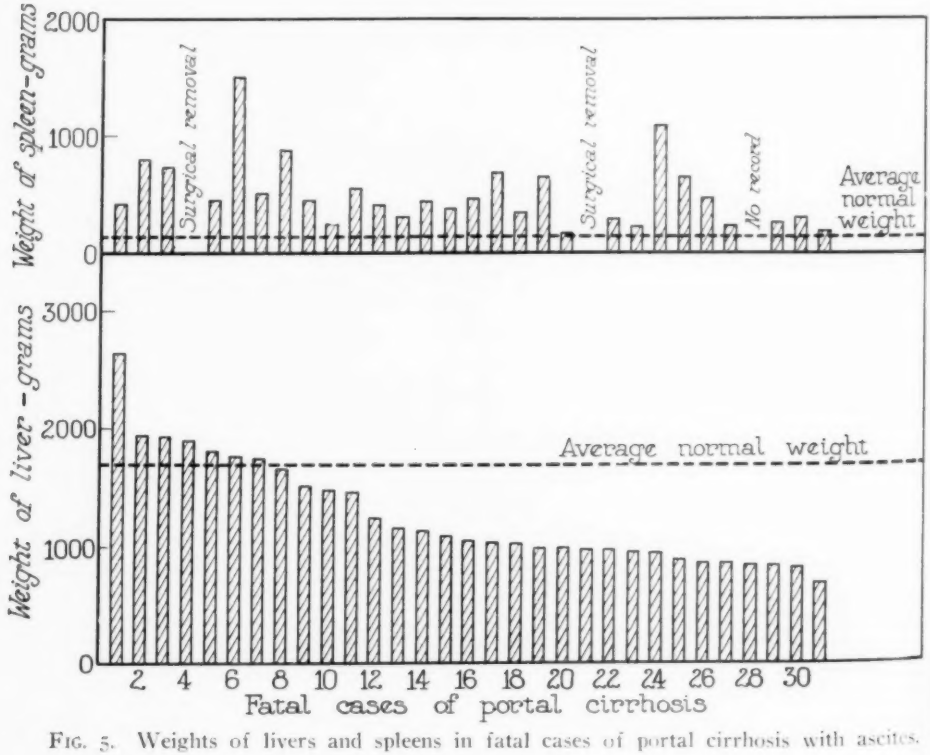

FIG. 5. Weights of livers and spleens in fatal cases of portal cirrhosis with ascites.

Active tuberculosis was not found in any case in this group, although healed lesions of tuberculosis were fairly common. Hydrothorax was found in an occasional case and terminal bronchopneumonia was present in about fifteen per cent. Anatomic changes in the kidney were uncommon. This seems significant when it is recalled that many of these patients had failed to respond to diuretics, either at the clinic or elsewhere.

Treatment

In the past, the treatment of portal cirrhosis has been directed largely toward removal of ascitic fluid, and there are reasons for believing that the strenuous efforts made in this direction have done much to shorten the life of these patients. It must be admitted, however, that many patients are sufficiently improved by removal of fluid to make the therapeutic attempts along these lines attractive. When one considers the natural course of cirrhosis, and the experimental evidence showing that ascites is an extreme terminal development rather than an essential element of the disease, the possible fallacy of giving ascites first consideration in treatment is obvious. This was noted by Morgagni[35] who asks this significant question: "Why should the physician trouble with very strong and violent remedies those in regard to whom he ought to think only how to preserve their lives as long as possible instead of attempting to cure their disorder?"

Treatment in portal cirrhosis should be directed primarily toward the detection and eradication of etiologic factors, and secondarily, toward the maintenance of the functional integrity of the hepatic cell. It is unnecessary to emphasize the fact that treatment antedating the development of ascites is highly desirable. Success will depend largely on the physician's ability to do these things, and, in the later stages, on the ability of the patient to respond to treatment by diuretics or to surgical measures.

The details of treatment in this group of 112 patients with decompensated portal cirrhosis have been considered elsewhere.[9] Prior to registration at The Mayo Clinic, treatment of these patients had been confined largely to paracentesis. A few patients had been given diuretics. After registration, eighty-four of the 112 patients were treated with mercurial diuretics combined with ammonium salts in large doses, after the method described by Rowntree, Barrier and Keith.[15] All of these patients were given a high carbohydrate diet, and water and salt were markedly restricted. About eighty per cent of the patients in this group responded satisfactorily to treatment: in forty-seven per cent the results might be classified as excellent; in about thirty-two per cent they were moderately satisfactory, and in twenty-one per cent they were poor.

Not all patients are suitable for diuretic treatment, and careful selection must be made. Patients with ascites of long standing may be resistant to even the most vigorous treatment, and too much must not be expected of diuretics in the late stages of the disease. In many instances, as the disease progresses, there is gradual

decline in the effectiveness of diuretics. Elderly and cachectic patients should be treated with caution, if at all. In the presence of marked jaundice, diuretic treatment is rarely effective, and should be employed only with great care. Active gastro-intestinal bleeding and mental symptoms also appear to be contra-indications.

Toxic reactions to treatment do not necessarily preclude further treatment, but they do emphasize the necessity for proceeding cautiously. Feissinger and others[13] have stated that if patients are not improving from the use of diuretics they are probably getting worse, a point which has been substantiated in my experience. Frequent paracentesis does not furnish an adequate substitute for treatment by diuretics. The intervals between tapping become progressively shorter and as White[50] has remarked, many patients do not survive even the second paracentesis. The effect of diuretics seems to be more permanent, for reasons which are unexplained. Saxl[48] and Feissinger[13] expressed the belief that in selected cases mercurial preparations stimulate hepatic regeneration and improve hepatic function. The best protective measure in the presence of hepatic lesions, both experimental and clinical, is the administration of carbohydrate by mouth and by vein. The daily use of glucose intravenously has given excellent results in the treatment of impending hepatic insufficiency, and deserves more general trial. Concentrated solutions of glucose (from 20 to 30 per cent) are particularly useful because of the small amount of fluid introduced. Such solutions may be given daily, in amounts of from 250 to 500 c.c., without apparent harm or discomfort to the patient, and in some instances they appear to have been life saving. The giving of insulin at the same time does not seem to be an advantage. When diuretics do not act, it is usually advisable to begin the forced administration of glycogen-forming substances and to perform paracentesis as often as necessary, to control the accumulation of fluid.

Operations. Surgical measures in cirrhosis have been designated to relieve the patient of ascites by mechanical means, to establish additional connections between the portal and the general circulation, to reduce the load on an overburdened portal circulation, and finally to eliminate channels of collateral circulation at vulnerable points, such as in the lower part of the esophagus. All of these procedures have given variable results and have not been entirely successful. The experience of surgeons in this field has been well covered by the papers of Hughson,[22] Höpfner,[21] and W. J. Mayo.[32] The various procedures which have been employed are represented schematically in figure 6. The Talma-Morison omentopexy, which has been so widely used, is accompanied by high immediate mortality, but it has given some fairly good results. Reisman[19] described two cases in which the patients were apparently cured by this means and some gratifying results have been reported from The Mayo Clinic. Hughson's[22] figures are not encouraging. Höpfner[21] expressed the thought that not more than one-third of patients derive any

benefit from this operation, and this has been the experience of Eliot and Colp.[19]

Splenectomy, which produces such excellent results in Banti's disease, does not appear to be so effective in portal cirrhosis. The differentiation between Banti's disease and portal cirrhosis is often difficult, and doubtless the two diseases are frequently confused. There appears to be a group of young persons with marked splenomegaly and hematemesis who are benefited by removal of the spleen, and in them definite portal cirrhosis is frequently found at operation. It will be noted, in figure 5, that the average splenic weight in twenty-eight cases of cirrhosis in which the patients came to necropsy was low, and it is difficult to see how removal of these spleens could have altered greatly the course of the hepatic disease. Splenectomy, of course, removes a substantial burden from the portal circulation, but the surgical

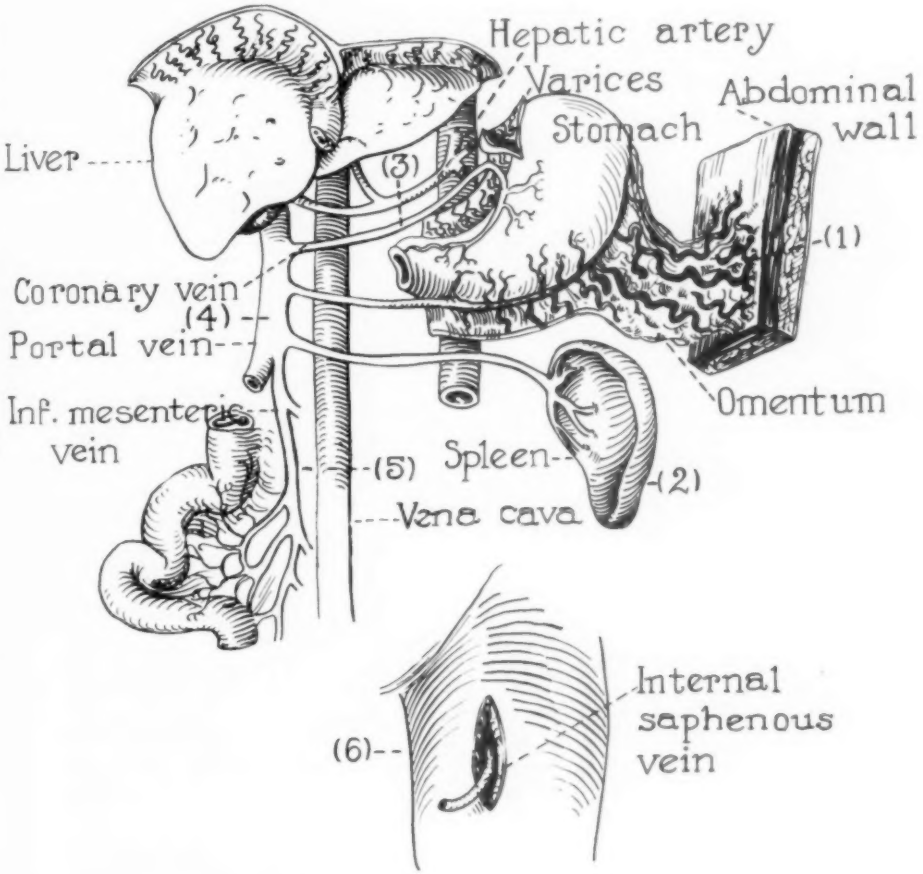

FIG. 6. Surgical procedures in portal cirrhosis: (1) Talma-Morison omentopexy, (2) splenectomy, (3) ligation of coronary veins, (4) Eck fistula, (5) anastomosis of inferior mesenteric vein to vena cava, (6) transplantation of saphenous vein into peritoneal cavity.

risk is considerable and the end-results are not altogether encouraging.

Ligation of the coronary veins of the stomach, either alone or in combination with splenectomy or omentopexy, has been done successfully[46] in a few selected cases, with good results. The operation is primarily directed toward the control of bleeding from esophageal varices and deserves a more extended trial. Various forms of anastomosis between the portal and venous circulation have been advocated, notably the Eck fistula[19] and anastomosis between the mesenteric vein and the vena cava.[5] Some good results have been reported, but in many cases sufficient connection between the portal and general circulation exists to render these operations more or less unnecessary. Various mechanical measures also have been proposed to rid the patient of ascites. Of these the most popular seems to be the method of Ruotte,[47] who has transplanted the saphenous vein into the peritoneal cavity. Success has been reported in some cases[33] and the operation recently has been advocated again by Franke.[14]

Most surgeons who have had large experience with the surgical treatment of portal cirrhosis feel that all types of operative treatment are carried out too late to be of much benefit to the patient. At the present time it is the general practice of physicians to try a variety of remedies before considering surgery. Knowledge of the usual course of cirrhosis makes the inadvisability of this plan obvious. If patients do not react to diuretics, and are progressively failing, it is unlikely that they will experience any relief from operation. If patients are young, in good condition and respond well to diuretics, omentopexy or splenectomy should be seriously considered. If hematemesis is a prominent feature, ligation of the coronary veins may be carried out with good prospects of relief. Even with the best selection of cases the surgical risk is not to be disregarded, and one must be prepared for many discouraging failures.

Summary

In reviewing a group of approximately 400 patients with portal cirrhosis in all recognizable stages of the disease, the chronicity and latency of the condition before the development of ascites is striking. Of patients with cirrhosis who are seen, the number of those who are in the preascitic stage is perhaps twice as great as the number of those who are in the ascitic stage. In the earlier stages, when these stages can be detected, eradication of causative factors may stop the progress of the disease. This is particularly true when alcoholism, syphilis, cholecystic disease, or chemical poisoning are causes.

The early symptoms are largely those of vague indigestion, intermittent jaundice, or gastro-intestinal bleeding, and in cases in which these complaints are made, tests of hepatic function may reveal the diagnosis. The earlier recognition of cirrhosis is highly to be desired because, in the earlier stages, arrest of the process is theoretically possible.

The appearance of ascites marks a critical point and indicates the end-stage of a lesion of ominous prognostic significance. Treatment in this

stage has been facilitated by the use of mercurial diuretics, and review of the results obtained in a series of 112 cases with ascites shows longer duration of life than in comparable groups reported in the literature. The indications for medical and surgical treatment, and the limitations of each, are considered with reference to the known course of the disease.

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Hereditary Ectodermal Dysplasia of the Anhidrotic Type*

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In making a report of this case which we feel belongs to the group described by Goeckermann[6] in 1920, MacKee and Andrews[12] in 1924, Weech[24] in 1929 and Jean Smith[18] in 1929, it is deemed hardly necessary to review in detail the cases comprising the list that has been so ably brought up to date by the authors mentioned.

We therefore will give a detailed description of this case and give tables of the chronology and clinical and pathological features to conform to those in MacKee and Andrews'[12] work in order to give uniformity to the reports of cases to date.

This chronological table is compiled from those given by MacKee and Andrews[12] and Jean Smith[18] with the addition of two cases described by Oliver and Gilbert[14] in 1926. After a study of the cases reported by Mackay and Davidson[13] as "Congenital Ectodermal Defect", they were not considered to have a place in this group which Weech[24] terms Hereditary Ectodermal Dysplasia of the Anhidrotic Type. Jean Smith[18] believes this a better term for the anomaly

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Table I
Reported Cases Arranged Chronologically

1.	1848	Thurnam[22]	male	English
2.	1848	Thurnam[22]	male	English
3.	1848	Williams[27]	female	English
4.	1883	Guilford[7]	male	American
5.	1898	Ascher[1]	male	German
6.	1898	Ascher[1]	male	German
7.	1902	Tendlau[20]	male	German
8.	1911	Wechselmann and Loewy[23]	male	German
9.	1911	Wechselmann and Loewy[23]	male	German
10.	1913	Christ[2]	male	German
11.	1915	Gibbs[5]	male	English
12.	1915	Gibbs[5]	male	English
13.	1918	Strandberg[19]	male	Swede
14.	1920	Goeckermann[6]	female	English
15.	1924	MacKee and Andrews[12]	male	Jewish
16.	1926	Oliver and Gilbert[14]	male	Polish
17.	1926	Oliver and Gilbert[14]	male	Polish
18.	1929	Weech[24]	male	Jewish
19.	1929	Weech[24]	female	?
20.	1929	Smith, J.[18]	male	English
21.	1929	Falconer[4]	male	English

and we agree with her reasons for the use of the title.

MacKay and Davidson's[13] cases showed dystrophy of the hair and nails only, with no change in the sweat or sebaceous glands and none of the other features of the anhidrotic type. These authors present a genealogical chart of affected persons in five generations in which transmission by both sexes is shown.

To this group we feel should be added Clouston's[3] analysis of 119 cases in six generations, reported under the title of "Hereditary Ectodermal Dystrophy". These are all dystrophies of the hair and nails and Clouston[3] differentiates this type from the anhidrotic type. He found in this group cases of keratoderma palmaris et plantaris and thinks they are residual forms of a disappearing dystrophy. This type involves the epidermis itself, the hair, nails, sebaceous glands and to some extent the sweat glands.

It is possible that there is some relation between the two groups.

The two cases reported by Oliver and Gilbert.[15] while not having all the major defects, are considered by the authors to belong to this group.

Case Report

Patient, G. F., female, aged 17, native of Detroit, born of Russian Jewish parents, has been under our care for ten years. Her *chief complaint* was deficient growth of hair and teeth and inability to sweat. Difficulty in working during hot weather.

Present Illness. Patient has noted that her hair was sparse very early and sought medical advice at that time. She was under treatment for a very short time when she discontinued same. In May, 1930, she again sought medical advice in an attempt to remedy her complaints.

Family History. Father is living and well. Mother died of heart disease and diabetes at 43. Two sisters and one brother are living and well. No history of a similar disease in the family. One sister, age 25, has absence of a few upper teeth with one peg-shaped upper left cuspid. Paternal uncle has manic-depressive psychosis.

Past History. The patient has had measles, chickenpox and scarlet fever. Tonsillectomy was done ten years ago. In the past two years her cervical glands became swollen and at that time were painful. In winter these glands swell up once a month and remain so for a few days. She has frequent nose bleeds. There is a history of convulsions until ten months of age. She was delivered by instruments. History by systems is negative.

Physical Examination. Height five feet, five inches. Weight, 124½ pounds. Blood pressure, 120/70. There is a peculiar lack of hair on scalp and face (eye-brows), axillae and pubis. Hair which is present over scalp and pubis has appearance of lanugo hair and is very scant, fine, dry and almost crisp and close to skin. *Skin* around upper and lower eyelids is pigmented. Lips are thickened. Skin is dry, cool and scaly in places. Face presents freckles. Forearms show faint brownish pigmentation over extensor surface. Eyebrows are lacking excepting a few hairs at midline. There is no hair in the axillae or on forearms and legs and but few hairs on mons Veneris. The eyes are small and set close together. The pupils are large, round and equal, react to light and accommodation. The nose is of a marked saddle-shape and the nares small. Foul odor of ozena comes from the nose and upon examination with speculum the septum is found to be partially destroyed. Grey necrotic material is present. The mouth is narrow, the lips prominent and thick, and the mouth is poorly kept. The teeth are in poor condition. Though but one has been extracted, one notes the absence of a large number. Those that are present are of a peculiar shape (peg-shape) and misplaced so that it is impossible to tell which are missing. The buccal membranes appear to be healthy. There remains a left tonsil tag. The neck glands are negative.

TABLE II
CLINICAL FEATURES OF REPORTED CASES

Clinical features	Oliver and Gilbert 1926 John Z	Oliver and Gilbert 1926 Joe Z	Weech 1929	Weech 1929	J. Smith 1929	Falconer 1929	Gordon and Jamieson 1931 G. F.
Age	10	16	14	7	5	6	17
Sex	male	male	male	female	male	male	female
Race	Polish	Polish	Jewish	?	English	English	Jewish
Number brothers and sisters	3	3	2	2	3	2	3
Number brothers with ectodermal defect	1	1	1	0	0	0	0
Ectodermal defects in antecedents	0	0	0	2 paternal great uncles with defective teeth	0	0	0
Diseases in antecedents	none	none	....	none	....	tabes in father	0
Married or single	single	single	single	single	single	single	single
Number of children	0	0	0	0	0	....	0
Serious diseases	none	none	none	none	none	....	none
Mentality	normal	normal	normal	....	normal ?	normal	normal
Sweat	none	none	none	yes	none	none	none
Suffers from heat	yes	yes	yes	no	yes	yes	yes
Scalp hair	sparse fine dry	sparse	sparse fine dry	sparse fine dry	sparse	sparse colorless down	sparse fine dry
Beard and mustache	none	none	none	none	none	....	....
Eyebrows	none	scant	sparse	scant	scant	none	sparse
Eyelashes	present	present	sparse	scant	scant	scanty	scanty
Auxiliary hair	none	....	none	none	none	none	sparse
Pubic hair	none	beginning	scanty	none	none	none	scanty
Lanugo on body	....	....	none	....	none	yes	scanty
Supraorbital ridges	....	....	yes	yes	yes	....	yes
Saddle nose	no	no	yes	no	yes	no	yes

Chronic rhinitis	no	no	yes	no	no	yes	yes
Papular face lesions	....	....	yes	no	....	yes	no
Pseudorhagades	....	....	yes	....	....	yes	no
Sense of smell	yes	....	....	....	....	....	yes
Sense of taste	....	....	....	....	....	....	yes
Mongolian facies	....	....	....	....	yes	?	yes
Deformed ears	....	....	small	no	no	....	no
Lips	....	....	thick everted	thick everted	thick everted	thick everted	thick everted
Vermillion border	....	....	well defined	poorly defined	well defined	....	fairly well defined
Teeth upper	normal large incisors	front malformed	4	5	6	2	7
Teeth lower	normal	normal	3	4	4	0	6
Unerupted teeth	0	0	0	0	0	0	0
Deciduous teeth	0	0	0	9	4	....	0
Deformed teeth	0	front	0	....	2	....	
Palms	....	....	normal	normal	....	thick hard	smooth dry hard
Soles	....	....	normal	normal	....	....	smooth dry hard
Finger nails	normal	normal	normal	flat concave	normal	....	normal normal
Toe nails	normal	normal	normal	flat	normal		
Genitals	normal	normal	normal	normal	normal	underdeveloped	normal
Mammae	normal	normal	normal	normal	normal	none	poorly developed
Gross appearance of skin	smooth dry	smooth dry	smooth glossy fine dry	normal	parchment thin	dry smooth	thin smooth glossy dry
Musculature	normal	normal	normal	normal	....	....	normal
Wassermann	negative	negative	negative	negative	negative	negative	negative
Basal metabolism	plus 9.6	....	minus 10	plus 42	....	....	minus 15

FIG. 1. Photograph of patient in 1920.

TABLE III
MICROSCOPICAL FINDINGS IN SKIN IN REPORTED CASES

	Oliver and Gilbert[14]	Weech[24]	Weech[24]	J. Smith[18]	Falconer[4]	Gordon and Jamieson
Location	none reported	none reported	none reported	anterior chest and axillary line level with nipples	thumb	inguinal region
Sweat glands	none reported	none reported	none reported	none	none	none
Hair follicles and arrectores	none reported	none reported	none reported	none	none	none
Sebaceous glands	none reported	none reported	none reported	none	none	none
Epidermis	none reported	none reported	none reported	no description	well differentiated and high degree of keratinization	layers normal
Derma	none reported	none reported	none reported	none	normal muscle fibres well developed	normal
Elastica	none reported	none reported	none reported	none		normal

The thyroid shows a small adenoma. The areolae of the breasts are 7 mm. in diameter. The breasts are flat and poorly developed so that very little breast tissue can be palpated. Otherwise the chest is negative. The abdomen is normal.

The patient presents a facies of a Mongolian type and looks anything but intelligent but upon questioning her one finds that she is above the average at school. She is seventeen years of age and in the 11th A grade. She plays the piano well. Her voice is husky, dry and squeaky. All *Reflexes* are normal. The arms well formed and shaped; fingers pointed; legs well formed and shaped. On the right knee there is a scar from injury.

Provisional Diagnosis at onset: Congenital lues and Hutchinsonian teeth.

Laboratory Data: Urine negative. *Blood Wassermann negative; Spinal fluid Wassermann negative.* Spinal fluid showed a negative cell count. Blood count on May 15, 1930: hemoglobin, 83%; red blood cells, 3,910,0000; white blood cells, 16,800; polymorphonuclears, 79% lymphocytes, 14%; eosinophils, 4%; mononuclears, 3%. On Oct. 6, 1930 the blood count was: hemoglobin, 80%; red blood cells, 5,370,000; white blood cells, 9,500; polymorphonuclears, 50%; lymphocytes, 41%; mononuclears, 7%; basophils, 1%. The electrocardiogram was normal. Blood chemistry findings on Oct 5, 1928, were as follows: blood sugar, 0.100; NC.N, 28.6; cholesterol, 136. On Oct. 13, 1928: blood sugar,0.095; Ca 8.4. Phos. 2.78. On Oct. 17, 1928: uric acid 4.28. B.M.R., Oct. 9, 1928, minus 11%. Repeated B.M.R., Oct. 11, 1928, minus 11%. Oct. 20, 1928, minus 20%. Goetsch skin reaction, Oct. 14, 1928, normal.

Histologic Description of Skin (Udo J. Wile, M.D., Professor of Dermatology, University of Michigan): The epithelium is about normal in thickness. Here and there on the surface is a patch of hyperkeratosis. The various layers of the epidermis are normal. The stratum granulosum is ill-de-

FIG. 2. Front view of patient, taken in 1930.

FIG. 3. Side view of patient in 1930.

fixed. The hematum and eosin specimen shows a fairly dense subcutaneous tissue with considerable fragmentation of the collagen bundles. The striking feature of the subcutaneous tissue is the complete absence of both hair follicles, sebaceous glands, and sweat coils and ducts. The Van Gieson stain shows the collagen bundles well defined, but distinctly fragmented. The subepithelial elastica is well stained, and shows no abnormality. The resorcin-fuchsin, lithium carmine preparation shows the elastica well distributed throughout the section and apparently no diminution or fragmentation of the collagenous bundles, and a complete absence of the entire pilo-sebaceous system and of the sweat coils and ducts.

Description of the Teeth (H. F. Doane, D.D.S., of Detroit, Michigan): X-ray examination was made on March 24, 1931. This examination consists of eleven intraoral films. At the present time the upper arch contains seven teeth and the lower arch five teeth. The patient gives a history of having had the lower left molar extracted. So far as can be determined, thirteen teeth are all the patient ever developed. None of the teeth which have erupted present the usual anatomic features. The upper right and left molars appear as bicuspids with an extra cusp; that is, the occlusal surface does not present the usual grooves and cusps of a molar. The appearance is very similar to the occlusal surfaces of the bicuspids, with the exception of the fact that there are two buccal cusps instead of one. The tooth occupying the lower right molar region presents anatomical features almost identical with the bicuspid. The roots of all molars appear single, although there is more than one root canal, indicating fused roots instead of the normal bifurcations. The teeth occupying the normal position of the upper central incisors present anatomical features very similar to the upper cuspids. The remaining seven teeth appear as the so-called peg teeth, their crowns being cone-shaped and presenting little or no anatomical marking. The tooth occupying the upper left lateral incisor region appears to be deciduous. At this time, its root is resorbed

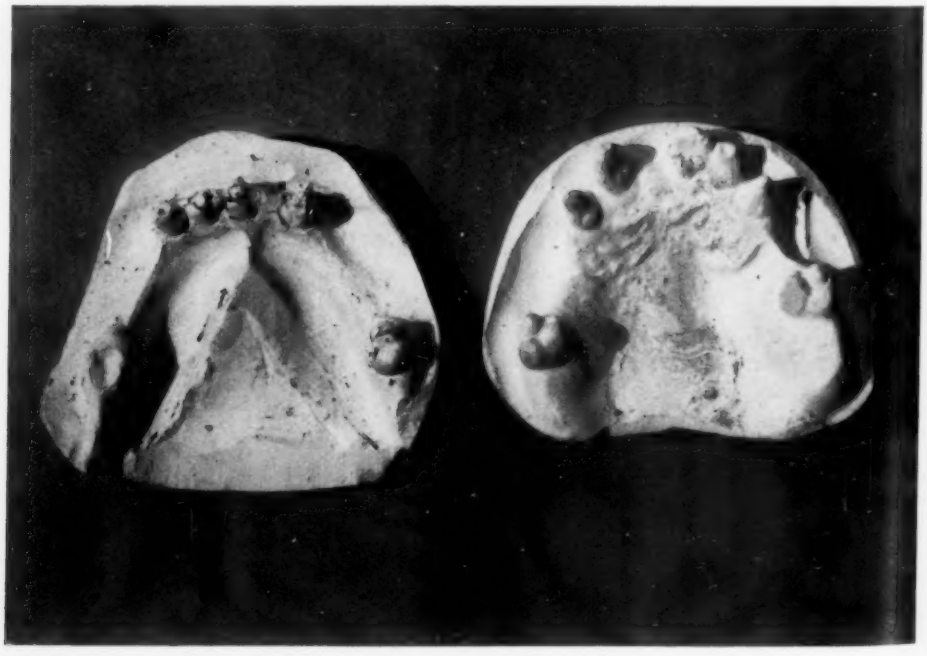

FIG. 4. Casts of teeth made by Sidney Rattner, D.D.S.

and the tooth is very loose. The enamel of the teeth which have formed and erupted is of usual thickness, but to date no microscopic study of tooth tissue from this patient has been made. Clinically and roentgenographically the structure of the enamel, dentine, pulp chambers and pulp canals appears as usual. Neither the extraoral nor the intraoral films of the patient's jaws reveal any evidence of unerupted teeth, and no tooth buds or malformed tooth tissue is evident. In the upper right bicuspid region we note an area of decreased density which appears to be poorly calcified bone. A similar area, but less extensive, is shown in the upper left bicuspid region. Roentgenologically, the bone in the lower right and left bicuspid regions, where no teeth ever developed, appears somewhat compressed, as compared with the regions in which teeth have developed. Otherwise the body structure of both jaws is quite usual in appearance on X-ray examination.

Discussion of General Changes Found on Skin and Appendages

The hair of the scalp was fine and grew sparsely over the entire scalp. It seemed to be of a normal length but was of soft texture and grew slowly. The eyebrows were lacking except at the inner third where a few hairs were found. The eyelashes were few and scattered along the border of the eyelids.

A few short, fine axillary hairs could be detected on close examination, as well as a very slight lanugo growth on the body, arms, upper lip and cheeks. This growth was practically invisible without the use of a magnifying glass. Pubic hairs were scanty.

Supraorbital ridges were prominent. No pseudorhagades were found but the vermillion borders of the lips were definite though not marked. The sense of smell and sense of taste were stated to be normal.

The bridge of the nose was depressed in the typical saddle-back formation; a chronic rhinitis was present with an accompanying foul odor. The general impression of the face was that it was of the Mongolian type.

The palms and soles presented many fine criss-crossed lines, were smooth, dry and shiny, giving the feeling of a dry skin tightly stretched over underlying structures. The finger nails and toe nails presented no abnormalities.

In the center of the back over the spine of the interscapular region and also over the scapular areas were three groups of minute papular lesions of non-inflammatory type suggestive of keratosis pilaris.

The entire skin was very white, fine, smooth, soft, glossy, pliable and dry.

Summary

A case is described presenting the major defects of anhidrosis, alopecia, dental aplasia, nasal rhinitis and saddleback nose with absence of sudoriparous apparatus.

Tables are presented with cases reported in the literature in chronological order up to the present time. A tabulation of symptoms of those reported since 1924 and a tabulation of microscopic pathologic findings are also given.

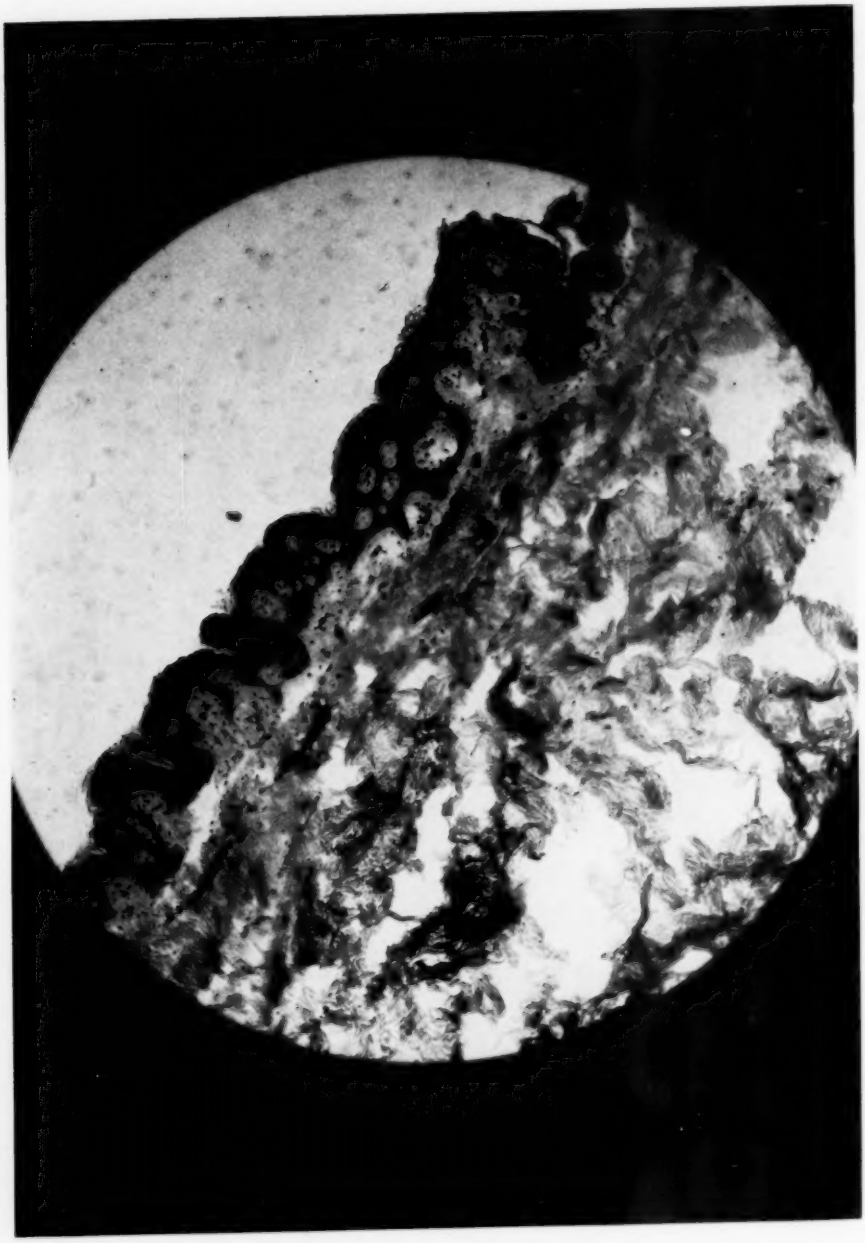

FIG. 5. Low power magnification of skin.

FIG. 6. Higher power magnification of skin. The entire pilo-sebaceous system is absent.

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The Application of a Modified Psychiatric Approach in the Treatment of Certain Gastro-Intestinal Disorders*†

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IT has long been recognized that a large number of patients who come under the care of the gastro-enterologist are psychoneurotic and one wonders whether the gastro-enterologist is able to treat these patients satisfactorily or whether they can be better cared for by a psychiatrist. A consideration of the type of psychoneurosis, its duration, its status praesens, etc., makes this decision less difficult. In those instances in which the psychoneurosis is very mild and is referred to the gastro-intestinal tract, particularly where the patient is fifty years or older, it is our opinion that a more satisfactory outcome can be obtained if the patient is under the control of a capable gastro-enterologist.

A gastro-enterologist should be thoroughly familiar with psychiatric measures if he hopes to succeed in caring for these patients. On the other hand, we are convinced that a capable psychiatrist cannot be expected to be a gastro-enterologist. In either event it is conceded that the individual patient must be considered primarily but the best and most permanent results according to our experience, are obtained by the physician whom we may call the gastro-psychiatrist. The latter sees no reason for unearthing complexes, delving into the subconscious and thereby magnifying the patient's troubles. He has no objection to the simultaneous use of both medical and psychotherapeutic forms of treatment. He is not aware of any danger in administering a medicinal treatment to a psychoneurotic nor does he decry its supposed detrimental effect. He does not stress too strongly the "nervous" element in the patient's personality because he knows from experience that little or no benefit is derived from such a procedure. He does not hesitate to treat the disease and to give the patient symptomatic relief while he studies the individual as a whole for he realizes through a long-continued association with these individuals that this plan inspires more profound confidence, and that it leads to a so-called cure which is more lasting and less time-consuming. Above all, he avoids deception and yet he employs a practical psychotherapy which neither

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stamps the patient as psychopathic, nor allows him to consider himself entirely normal.

How does the gastro-psychiatrist study his cases? He, of course, realizes that treatment, as well as disease, cannot be standardized. He therefore makes the usual complete study including a good history, a brief personality study, a physical examination, the indicated laboratory procedures and any special studies which seem advisable. All these he considers essential parts of psychotherapeusis. If after such a thorough study no organic basis for the patient's symptomatology is noted he can offer reassurance in a manner which is most convincing. In this way he not only gains the patient's confidence but makes the first step in the needed reeducation. In his conversations much is learned concerning the patient's reactions and this aids in pointing out the correct plan of treatment. The symptoms are genuine and if drugs will relieve these, they are temporarily employed without fear of dire consequences. Rest, diet, exercise, occupational therapy are utilized as indicated. Where hospitalization seems advisable a general hospital or sanatorium is selected depending upon the status of the patient. Sometimes a change in environment alone is a most valuable therapeutic measure. It is surprising how willing a patient is to cooperate with a gastro-psychiatrist and how frequently the former gradually learns that "nervousness" is the etiologic agent in his disturbance. In such instances, he will frequently request treatment for this symptom instead of having it forced upon him. At this stage of a sympathetic yet firm relationship between physician and patient the factors concerned in the latter's maladjustment are unraveled with much less difficulty. We have seen the most sensitive patients gradually become desensitized by such an approach and more extraordinary is the fact that the sequence of events leading up to the present illness explain themselves automatically. There is, however, a certain group of individuals who do not respond so well. These are usually cases who have consulted many physicians, going from one to another without allowing time for sympathetic understanding and adequate treatment. However, in some instances, even such individuals have been helped by the procedure which we advocate. Often the mental effect of a complete examination with an explanation of the condition and reassurance results in a "cure". For example, this occurred in many patients who presented themselves with a cancer phobia and in whom this idea was not only recognized early but dispelled as a result of a complete study.

In many of our cases we have observed that with individuals who lack average intelligence the response to psychotherapeutic measures is unsatisfactory, whereas the treatment of a symptom or an organic condition (if that exists) is impressive and in itself becomes an efficient psychic measure. For instance, the mere application of a support in a patient with enteroptosis or pendulous abdomen, even though these conditions may have little to do with the production of symptoms, gives such great physical comfort that general improvement follows. Many

other examples could be noted but the idea which we wish to emphasize is that this group does not lend itself to pure psychic appeal for there is little to appeal to. On the other hand, these individuals respond to medicine and physiotherapy because these measures inherently carry with them suggestive properties.

Witness this instance, related by Bland Sutton,[1] of a psychiatrist who made excellent use of a frog in the following circumstance. "A thin and foolish woman believed she had accidentally swallowed a frog and that her thinness was due to the frog eating the food in her stomach. In order to dispel the illusion the doctor gave the patient an emetic and during the vomiting he slipped a frog into the basin. When the patient saw the frog her joy was great, but in a few minutes her depression returned. 'Oh!' she exclaimed, 'I am sure this frog has left some young ones in my stomach.' The doctor looked wise, pulled out his magnifying glass, and after critically examining the frog said unto the patient, 'Fear not, this frog has not left any froglets inside you; behold, it is a male!' The patient was quite satisfied, became happy and in a few months was plump again. She was not a naturalist, and therefore ignorant of the fact that it is difficult to tell the sex of frogs by mere inspection except at the breeding season."

We should like to direct attention to another group of cases in which any form of psycho-analysis is contraindicated. When a patient is examined one often realizes that no progress will be made unless personal matters are investigated. However, there have been many individuals who consulted us after they had bitterly resented what they deemed irrelevant and unnecessary questioning directed towards their private affairs at the hands of psychiatrists. We have seldom found it necessary to inquire into sexual relationships, marital incompatibilities, financial affairs, social and religious difficulties. In some cases the patient is aware of an underlying maladjustment and is able to combat it if his mental attitude is changed through a process of reassurance, encouragement and relief of symptoms. In other instances, the individual fails to recognize any underlying psychical causes and not only seeks but insists that a physical basis be discovered. In this group a tactful, delicate, and sympathetic approach opens up more avenues of willing discussion than could be obtained by the immediate attack upon repressions, inhibitions, the subconscious, and so forth. It is certain that every one of us has built up a defense mechanism which is the basis upon which our adjustments to our environments rest. To shatter these structures is dangerous. They are the buildings resulting from years of construction, tampering with them is unwarranted. Psychiatrists often seem unaware of this fact.

It is generally admitted, as Reynolds[2] states, that a fundamental principle of the treatment of neurosis is based upon an explanation to the patient of the evolution of his nervous symptoms from their original sources. In our experience, there are a large group of cases in which such explanations are best omitted. It is proper to ascertain the causative factors in-

volved in each individual case but it is not well to break down a moderately substantial foundation because one feels that the patient should conform with the majority. If we learn that the neurosis is dependent upon certain sexual problems, certain environmental conditions, certain physical handicaps, etc., these can be adjusted in many instances without the patient's knowledge and with much better effect. Many of these individuals gradually become self-explainers and their pride in having discovered and treated themselves is in itself a great conquest. Like the obstetrician we must preach "noli me tangere" in this group of cases which will become more and more well defined as time proceeds. We realize all the old arguments about the necessity for strengthening individuals with neuropathic streaks, inferiority complexes and unstable nervous equilibria but we know from an ever growing experience, that the best procedure is not to have the patient become conscious of his shortcomings.

Preventive medicine[3] plays its psychiatric rôle which is concerned among numerous other things, with the routine and regular overhauling of the type of the patient with whom we are concerned. It is on this account that we advise our patients to visit us at regular intervals. After all, who can determine exactly where the normal limits stop and the abnormal begin; where, for example, the micro-manic-depressive (Overstreet[4]) becomes the manic-depressive. If we are indulging in such vagaries let us give the patient the benefit of the doubt and let us not convince him and ourselves that he is mentally sick without due evidence. Just as the psychiatrist errs on his side, so the internist, as Reynolds remarks, "is liable to fail if he does not study carefully all the features of the case before starting to treat it". "The difficulty" he continues, "is that the medical practitioner is in danger of becoming so absorbed in the treatment of any obvious organic pathology that he may fail to pay attention to the neurotic symptoms which are its result. On the other hand, if the neurotic element is predominant, it is equally easy to overlook the apparently trivial physical abnormalities which may have been contributory factors in the disturbance of the nervous equilibrium. In order to steer a middle course between these two common errors, it is well to assume that every case has both an organic and a functional element."

It is generally known that most psychopathic persons with gastro-intestinal complaints (as well as society in general) fear the stigma of having any professional contact with a psychiatrist. Certainly this reaction should not exist but since it does, it is best to recognize it. We agree with Alvarez[5] that one must be fitted temperamentally for the problem presented by these patients. Since the gastro-psychiatrist is familiar with certain syndromes in his specialty it is more probable that he can evaluate the symptom-complexes and plan a rational form of treatment suited to the individual. He certainly realizes that there is a large group of cases in which the mechanism of the affection must be explained in order to obtain satisfactory results. Such an example

may be present in the following instance taken from Oliver[6]. "When a woman who has had phobia of cancer all her life and who has restricted her diet so that she is skin and bone because she has an idea that rough food irritates the stomach and produces cancer there,—when she can be brought to realize that her mind has been sensitized to the fear of cancer because of her distressing experiences with a beloved father who died of it—why, you have already robbed her phobia of a good part of its nameless overshadowing horror." He is also aware of those cases in which patients substitute one obsession, one disease, one anxiety for another. Jeliffe[7] has called attention to instances in which cures of various "diseases" were obtained sometimes with the aid of surgery only to have another and often less vulnerable affection arise. It must be understood that this method of treatment is offered only in a certain selected group of cases. There are patients with whom one must insist on the mental basis of the affection. Care must always be taken, however, not to plunge the patient into hypochondriasis (Dubois[8]) and one must always have "sized-up the situation" before proceeding in this manner.

To make our position clear, we do not claim a cure-all; we simply offer a method, not different in kind but in principle. In brief, we do not believe that the majority of these gastro-psychoneurotics are best treated by psychiatrists since from the very beginning, the former are antagonistic to psychiatrists and where antagonism exists good therapeutic results are wanting. In the treatment we aim, as far as possible, at prompt symptomatic relief. The relief of symptoms leads to a more pliant mental and physical attitude. The fear with which certain psychiatrists administer drugs is commendable in some cases but not, as a general rule, in gastric neuroses. Gastric symptoms can be relieved without the danger of formation of drug habits or other untoward effects.

In order to illustrate more clearly this modified medical and psychiatric approach 200 consecutive gastro-intestinal cases in our clinic were studied. Of these, fifty showed etiologic factors which were definitely psychogenic while in the rest the nervous element was more or less prominent. In every instance, however, the chief complaint was referred to the gastro-intestinal tract. Each patient was subjected to the complete study already mentioned; nothing was assumed. Upon the basis of this examination treatment was instituted.

A few abstracts of illustrative cases follow:

Case I. J. L. S., male, (a salesman) aged 60, complained of "stomach trouble and nervousness" of two years duration. The patient was aware of the fact that his mother had died of hypertensive heart disease. In the past he had had the usual childhood diseases with no complications but about ten years ago, following a so-called "mild stroke", he became very weak, requiring about three months before he fully regained his faculties. A review of the systems discloses the following important data:—nocturia, three or four times; very nervous; some insomnia, occasional spell of dizziness and weakness; tires quickly; has many obsessions. Little, except the enumeration of some vague digestive symptoms, could be learned of the present illness. In other words, there was a gastro-intestinal fixation.

On physical examination, the general appearance was one of depression in a well nourished and well-developed elderly man. Briefly, the positive findings were dilated pupils reacting normally, ophthalmoscopic examination normal, lungs normal. The heart was normal in size, the sounds were regular, loud and forceful. Blood pressure 200/120, with no constant associated symptoms. The radials were tortuous and moderately thickened. Abdomen normal. Reflexes normal. The mental examination disclosed many traits of the parergastic reaction type but anxiety neurosis seemed more likely. The urine showed one plus albumin, three plus glucose, a few hyaline casts and white blood cells. Other laboratory examinations were normal.

Our impressions were arteriosclerosis, hypertension, anxiety neurosis, questionable chronic nephritis and questionable diabetes mellitus. Hospitalization was advised. Further studies showed the "diabetes" to be of the nature of renal glycosuria, while no evidence of kidney damage was adduced.

The patient was seen daily, treated symptomatically, spoken to rationally and semi-analytically. Under the administration of mild hypnotics he rested quietly. Gradually his obsessions became less marked. At the same time he began to realize that his principal difficulties were due to "nervous" factors. As far as allowable we stressed his physical fitness, creating simultaneously a restful, reassuring environment and relief of symptoms. The patient, on the other hand, proceeded a step further and diagnosed his case "nervousness". Today, six months later, this man is back in business, working efficiently. He recalls that he was "slightly mentally ill" and is very thankful that we had prevented his relatives from sending him to a mental hospital. It is very unlikely that this patient will have another "nervous breakdown" but should this happen he will certainly seek immediate aid. At the age of 60 he is made fit to work in a certain environment by a mild sort of treatment lasting four weeks.

Case II. G. N. C., female, student, aged seventeen years, complained of "gas on stomach" and dizziness. The family and past histories are essentially non-contributory. The present illness dates back four years when belching was first noticed. For two years there were exacerbations and remissions but gradually the belching became almost continuous and this with a sense of dizziness and emotional instability have persisted to the present time. The physical examination was normal in every detail. The urine and blood were normal. The stool showed two plus mucus. She was unable to swallow the tube for a gastric analysis. X-ray studies disclosed no organic defects; the pylorus was spastic and the colon markedly prolapsed and spastic. In a casual but quite thorough mental examination no alarming findings were noted.

Our impressions were aerophagia, nervous indigestion, and a spastic gastro-intestinal tract. The patient was placed on a schedule of exercises with rest periods and a prescribed dietary regime. In addition she was given certain medicinal preparations combining sedative and antispasmodic properties. Aerophagy was explained to her. psychotherapy was made to appear incidental.

Under monthly observations a steady gain in weight has been noticed, she has become more stable emotionally and as she remarks, "feels almost well". No attempt was made to blame the entire condition on nervousness although the mechanism of aerophagia was explained in detail. The medications are gradually being reduced but without their psychic as well as medicinal effects, we feel certain that our success in this case would have been much less marked. The "cures" are not temporary since the patient returns at appointed intervals for a check-up and is not discharged until she has a well-established understanding of her difficulties. She is convinced that no organic disease exists and as each visit culminates, she realizes more and more that hers is a functional abnormality and gradually she concludes that it depends upon her emotions. The patient credits herself with this discovery and in this attitude lies strength. If the usual psychiatric approach were attempted in a reaction pattern of this kind the problem would have been much more difficult even if the patient's co-operation were taken for granted.

Case III. R. B., male, shoe-merchant, aged 31 years, complained of constipation and "stomach trouble" characterized by "panicky feelings" and nausea. The family history was non-contributory. In the past there have been four operations over a period of nineteen years. The patient has always been of a highstrung, excitable and unstable nature, smoking excessively and imbibing alcoholic beverages occasionally. The present illness is said to have begun three years ago when it was noticed that an already marked constipation was becoming more severe. Symptoms of dizziness, palpitation, "spots before eyes" and general unsteadiness were experienced, and the patient believed he was slowly being poisoned through intestinal stasis. Depression was well on its way but due to certain business matters his mind was occupied for some months. He managed to get along, building symptom upon symptom until six weeks ago when, following the extraction of a tooth, there was a little more than the usual amount of bleeding. He became extremely nervous and apprehensive; a multiplicity of symptoms appeared; his constipation became more uncontrollable than it had ever been; pains and aches were experienced throughout the abdomen; and nausea and loss of weight were noticed. He was on the verge of a mental collapse when seen.

On physical examination he was found to be of asthenic habitus, well developed but only moderately well nourished. He appeared worried and depressed. The head, heart and lungs were found to be normal. Blood pressure, 120/80. Pulse, 90. The abdomen was soft, semi-relaxed and with the exception of a hernial repair scar in the left inguinal region presented no abnormalities. The genitalia, extremities, skin, etc., were normal. Reflexes were very active. The urine and blood examinations were normal. The stool contained a considerable amount of mucus. The Ewald test breakfast showed a total acidity of 82, free hydrocloric acid, 65. The Wassermann reaction (blood) was negative; phenolsulphonephthalein test showed 55 per cent excretion in two hours (intramuscular injection); blood chemistry studies normal. X-ray studies revealed a prolapsed colon and stomach with a probable chronic appendix.

In addition to his mental upset, therefore, he had intestinal stasis, enteroptosis and a probable mucous colitis.

The patient seemed greatly relieved when told he had no organic lesion but he was advised to enter a hospital for treatment. The effect of a complete examination with a careful explanation of the condition and reassurance had not only gained his confidence but had already started him on the road to recovery. Correction of the constipation was achieved by means of diet, enemata, etc., leading finally to bowel re-education. In addition, rest, exercise and a well rounded daily routine including a requisite amount of diversion were employed and throughout, a sensible and unobtrusive psychotherapy was practiced. A rapid restoration to normal occurred.

This patient has been in communication with us by mail for a half year. He has gained weight steadily and seems to be getting along splendidly. From the tone of his letters we feel that we need not fear a "nervous breakdown" in the near future.

We must remember, as Alvarez[9] cautions, that "many of the people who complain bitterly of auto-intoxication symptoms are usually sensitive and keenly aware of what is going on in their bodies. It is this sensitiveness which distinguishes them from those who can go for a week quite unconscious of the fact that their bowels are crammed with feces." In addition all of us recognize the fact that "sensory impulses from the digestive tract can profoundly influence our emotions, our mental processes and our vasomotor balance." We recall the young woman who, although symptomless, was extremely frightened because she ordinarily had a bowel movement every five days and at the time of her visit to our clinic had not had a stool for eleven days. Her fears were allayed

after a thorough study and a corresponding effect was soon noticed on bowel function.

There is a group of patients who are so ill-informed about their illnesses that one feels it necessary to instruct them to some extent concerning the mechanics of the digestive tract. This is certainly a hazardous business but in our experience one of two procedures may be followed:—either give a thorough explanation of the condition or have it understood that the patient's ideas of the disease are erroneous and that its treatment is to be entrusted entirely to the physician in charge.

In the case of R. G. (*Case II*), female, aged 44, the complaint was referred to the stomach. She was found to have mucous colitis. It was explained that the examinations disclosed no organic disease but she could not be convinced that her symptoms could be due to a non-organic condition. She objected to our assumption that she was a very nervous woman. It was decided to study the case in the usual psychiatric fashion but recovery was slow, tedious and never quite satisfactory. This is to be compared with H. R. S. (*Case I*), female, aged 33, in whom the same situation was met. In this case no explanations were given but various forms of medicinal therapy in addition to diet and rest were employed. At each visit, we suggested that she was certainly much better as revealed by our examinations. Drugs, never given at random, were changed to relieve gas, spasm, intestinal stasis, etc. With this form of therapy, she was brought back to usefulness in a short time. These are examples of a large group of cases which we have observed and in our experience, the latter form of treatment is much more satisfactory not only as to its immediate effect but also as to the permanency of cure.

In *Case VI*, D. V. D., a very nervous young woman of 34 years with many vague digestive symptoms, the instructions given were briefly as follows: "Conditions of this type necessarily involve the nervous system and it is important in considering your case to recognize this factor. Any treatment, therefore, which is undertaken, should be directed not only to the digestive tract but equally as well to the nervous system. I should therefore advise you to continue with the dietetic regime (spastic colitis), which I have given you, get considerable rest, wear your abdominal support (enteroptosis with symptoms) and get a reasonable amount of exercise. Your surroundings should be bright and cheerful and you should try as far as possible to overcome all irritations. For the constipation mineral oil is useful. A nerve tonic is advisable and the administration of hydrochloric acid (achlorhydria) with pepsin is also very helpful. I know that you will do well and I shall be very glad to cooperate with you in any way I can to help you regain your health." This, with its implied suggestions, later to be gradually amplified, serves as a basis by means of which the patient acquires the method of studying her personality.

Case VII. B. M., female, aged 41 had always complained of gastro-intestinal difficulties. She had run the gauntlet of medical and surgical treatments. A complete study led to the belief that we were dealing with an unhappily married, pronounced hypochondriac whose greatest desire was to remain a chronic invalid. In cases of this type a complete psychiatric study is indicated and we therefore referred this patient to a competent psychiatrist who finally informed us that the patient would not cooperate with him and had decided to get another doctor. This type of individual often does not respond to any type of treatment and sometimes becomes institutional material. Another problem presented itself in the case of S. H. W., *Case VIII*, who had, in addition to a penetrating ulcer at the pylorus, a depressive psychosis which demanded institutional care. Here psychiatric and gastroenterologic cooperation was necessary.

Case IX. L. S., female, aged 20, complained of heartburn and a feeling of full-

ress in the epigastrium. A complete work-up led to the following impressions:—Aerophagia, enteroptosis, spastic colitis, intestinal stasis, and "neurasthenia". The patient was so emotionally upset that she was hospitalized since we felt that she could not, despite every effort, modify her mental state in her present environment. Subsequent studies revealed the fact that the patient's instability was due to a shock occasioned by the death of a very dear friend. To this she reacted with what she recognized as a gastro-intestinal upset. Her treatment consisted of reassurance, diet, rest and medicinal therapy (to relieve "heartburn" and "gas formation"). She gradually recovered and it was only after she was rid of her belching and constipation that the probable association with her friend's death was discussed. She reacted admirably.

Case X. W. R., male, aged 33, complained of "stomach trouble" with vague abdominal discomfort which he believed was due to his "nerves". After a thorough study he was told that he was organically sound and that he had what was called "nervous indigestion". It was explained that strict adherence to a prescribed regime and his complete cooperation would doubtless rid him of his difficulty. He responded well and when last seen it was clear that he recognized the mechanism of his gastro-intestinal upset.

Case XI. G. S., male, aged 27, presented a similar picture complicated by a subacute appendix. He feared an operation but after a week's observation, during which time the signs in his right lower quadrant remained quite definite, he submitted at our advice. Pre-operative and post-operative care were made to include sufficient analgesic preparations so that he would be spared the least pain. (He seemed to be mentally hyperesthetic). Today, three months after operation, he is getting along splendidly and remarks that his fear of pain has disappeared.

Case XII. E. I. F., male, aged 44, entered our clinic with many gastro-intestinal complaints which appeared when his home physician, during a periodic health examination, mentioned the necessity for ruling out cancer in certain cases. This suggestion was sufficient to set up a cancer phobia in this individual and unconsciously he reacted with the production of numerous gastro-intestinal symptoms. The examination by us disclosed a spastic colon which responded to antispasmodic therapy. Recovery, finally, was complete, when unsolicited, he was told emphatically that he "absolutely had no cancer".

Although emphatic reassurance is the coup d'etat, straggling symptoms must be treated since their persistence may cause some patients to doubt the physician's diagnosis even though they have utmost confidence in him. An instance of the latter is the *Case XIII*, M. S., female, aged 52, who was told by her physician that although her symptoms suggested gall bladder disease, examination seemed to indicate a normal organ. Her symptoms persisted, however, and she visited an esteemed clinic where she was informed that only immediate cholecystectomy would afford her relief. This frightened her greatly. Several months later the patient visited our clinic where she was found to be extremely apprehensive and to have a definite mild cholecystitis. She was reassured and when her organic disease responded readily to the method of non-surgical biliary drainages of Lyon, her apprehensiveness vanished.

Finally, *Case XIV*, is outlined briefly because it teaches so valuable a lesson. W. K., female, aged 42, is an example of that group of patients who talk incessantly of their symptoms and who unfortunately are immediately stamped as neurotics. As a matter of fact, careful examination often discloses an organic illness. W. K. had passed from one physician to another and in each instance was labeled "essentially neurotic". She was found to have a malignancy which later caused her death. This case impresses us with the importance of divorcing ourselves from preconceived notions; each patient demands and deserves a thorough examination.

Summary

To summarize briefly, we have attempted, in this paper, to stress several important points, two of which we should like to reiterate. The first, the

necessity of a thorough survey of the patient, is generally accepted, if not practiced. The second, the use of drugs in psychoneurotics, is neither generally understood nor accepted. We have tried to show that there need be no taboo on drugs used with reason, that they are very helpful and that they are often of more psychotherapeutic value than other more frequently employed measures. In our study, we have seen a varied assortment of reaction types derive striking benefit from the temporary and rational use of drugs to relieve symptoms. We have refrained from making any statistical report at present because investigations of this nature do not easily lend themselves to mathematical arrangements. At present we simply bring forth the fact that in a large series of cases with more or less "nervous" etiologic factors the results obtained are better when a practical psychotherapy includes in addition to the usual measures (reassurance, superficial analysis, physiotherapy, rest, massage, exercise, occupational therapy) the use of drugs to relieve symptoms. If drugs are used sensibly we need not fear that they suggest organic disease and thus give the patient a reason for complaining. However, we realize that this method is not applicable to all reaction-types. That there is a large group of cases where the mechanism of the reaction must be explained is agreed. On the other hand, it is a well recognized fact that the mental effect of a complete examination with an explanation of the condition and reassurance results in a "cure" in a large number of cases. As Lyon[10] has aptly stated: "By improving our methods of total diagnosis of a patient we thereby improve our chances of appropriately treating that patient from many angles instead of his chief major disease alone. The thoroughness of the total treatment is often the real secret of success."

We have introduced the term gastro-psychiatrist. The temperamental fitness of this individual differs greatly from the average psychiatrist or gastro-enterologist. He stresses neither the "whole" of the former, nor the "part" of the latter. He takes both into consideration *equally* and does not hesitate to cure the part while treating the whole. Not every gastro-enterologist and psychiatrist is suited for this specialty; they may practice it but not with all the attainable success.

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The Prestige of the Internist*

By Miles J. Breuer, M.D., F.A.C.P., *Lincoln, Nebraska*

INTERNISTS who are working in well-developed medical centers, on a basis either of referred work or of institutional work, are not frequently confronted with problems like the cases mentioned below. But from seventy-five to ninety per cent of the internal medicine of this country that is waiting and crying to be done conscientiously and scientifically, exists and awaits among the masses who do not have access to modern medical centers, whose medical conceptions are from fifteen to fifty years behind the forefront of modern medical thought, and who do not even know what an internist is. They do not understand the character of service involved in an "examination" as an internist means the word; have no idea of what a diagnostic study consists or what it can do for them. They just want a doctor. They came directly to the internist, and he must educate them to evaluate his services, or to be referred to other specialists.

Case 1., J. H., aged 55, traveling salesman, called the writer into his home on a number of occasions for the relief of acute abdominal pain. The principal therapeutic measure to which the pain responded was rest. On several occasions I advised this man that there was a possibility of the existence of a circulatory lesion not apparent to the type of examination that was possible on an emergency visit, warned him of the danger that might result from its neglect, and urged him to have a proper diagnostic study. He agreed with this, until it occurred to him to ask what the cost would be. When told of the probable cost of the necessary study and observation, he backed away in dismay. On several occasions he was willing to go to a hospital and be operated on, at a cost of from four to six times as much as the diagnosis would have cost; it took some rather firm dissuasion to convince him that he did not have a surgical lesion. After he found what the proposed examination might cost, he was very resentful and did not call me any more. One day he was found dead in his car, and the autopsy showed coronary stenosis.

Case 2 was seen in connection with a visit to a colleague in a neighboring city. A thin, pale young woman came to him, requesting some medicine for her kidneys because of a backache. He explained to her the need of a thorough diagnostic study in a case like hers, and was also met with the question of the probable cost of such a study. The lady did not return to him; but we happened to see her about a week later when she was brought into a hospital clinic, paralyzed and anesthetic from the waist down and with sphincters paralyzed. She had gone to a chiropractor and paid him in advance for a series of treatments a sum not substantially different from the one estimated by the internist as the approximate cost of an examination. Further examination showed that she had tuberculous caries of a vertebra with fracture and compression of the cord.

As a multiplication of cases like the above could demonstrate, the American public is not yet conscious of the

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internist as a new and different figure in medicine, who, on the one hand has a distinct type of service to offer differing considerably from "just going to a doctor and getting some medicine", and on the other hand who works under such conditions that there is a standard of expense connected with his services which also differs markedly from just "going to a doctor".

This lack of appreciation of the internist's function is not limited to the lay public. Just recently I received a friendly visit at my office from a man who ranks high on the surgical staffs of two hospitals and who has made a name for himself in a special field of surgery. I was showing him the records of a certain case, which at first had been diagnostically obscure, and afterwards had proved interesting enough to merit a thorough clinical study. He waved away my pile of records. "What do you want to do all of that for?" he asked in perfectly sincere deprecation; "Why don't you come right to the point?" His attitude is typically illustrative of that which I have found on the part of many medical men in our community, which has the reputation of being a progressive one.

The writer does not believe in emphasing the economic or business side of medical practice, and does not wish this article to be construed as a plea for some plan of bringing up the fees of internists. It is rather the expression of a desire to suggest the need of educating the public to understand the function of the internist, for the sole purpose of enabling the internist to function properly, and for no one's ultimate greater benefit than that of the public itself.

In this community, which is quite like ninety per cent of the rest of the United States, dentists and surgeons have already educated the public to a proper evaluation of their function, and to an acceptance of their standards of remuneration. The average man admits that the surgeon is perfectly justified in receiving a minimum of $100 to $300 for an operation. But, if someone should tell this same average man that the internist exercises quite as much skill and ability, assumes quite as much responsibility and that his services are of quite as much importance and value to the patient as in the case of the surgeon, he would be dubious and skeptical. He does not know enough about what an internist does, to form an intelligent opinion. And therefore, when an internist charges him a fee on a basis analogous to that of the surgeon or the dentist he is indignant and thinks he is being unjustly treated.

The reason for this is twofold. On the one hand the surgeon and the dentist have educated the public. Time and custom have succeeded in producing a willing acceptance of the situation. The public is reconciled to the cost and believes in the value of the service, and the surgeon and the dentist continue to develop their knowledge and their technic on a reasonably remunerative basis. On the other hand, there is a popular appeal about the accomplishments of surgery that is lacking in the humdrum, plodding procedures of internal medicine.

The public has a very poor knowledge and appreciation at the present time of some of the remarkable things that are being accomplished by internal medicine. Only a limited number of lay individuals are aware of the diagnostic marvels that our specialty has produced and of the therapeutic miracles that it is working. If the dissemination of such knowledge is left to the usual natural processes, it will be twenty years before the importance of electrocardiography and the magic of insulin are as much of a byword in the home as is appendectomy. Nor does the general public have any idea of the overhead expense involved in the diagnostic and therapeutic methods connected with internal medicine. Omitting entirely the consideration of the time and expense required on the part of the internist to acquire the necessary ability, what average layman has any idea of the overhead factors entering into the study of, for instance, a case with chronic epigastric pains and a loss of physical capacity; of the time and expenditure of lawyer-like skill necessary to extract the indispensable history, of the expenditures for laboratory work, the basal metabolic rate, the electrocardiogram, the x-ray, and the assistance of skilled technicians? The bill for a study of this sort stirs up the common man's resentment, because he cannot see what he has gotten for his money. Nothing illustrates this point better than the requests of many of these patients that they might keep their x-ray films; a desperate attempt to salvage something concrete and objective as a symbol of what they get for the money they have paid out.

This attitude, of course, makes the work of an internist difficult. Naturally, in response to it, he makes some concessions. Either he omits work that ought to be done, or he does without charge work for which he ought to be paid. Either course handicaps the freedom of his scientific activities, unless he is fortunate enough to be practicing among a wealthy clientele; and this article is being written about the seventy-five or ninety per cent of internists and near-internists who are not so situated. From the very beginning of the study of such a case, the internist feels under constraint; he knows that a financial argument is coming, and the thought interferes with the proper freedom of his efforts. It is not a question of whether or not the internist makes money. It is a question of providing him with the opportunity to study his cases adequately under a condition of affairs where the work must pay for itself. Under the present social organization, most of our internal medicine is being done by men or groups who are not endowed and have no independent source of income. If the patient does not pay for the work, in the total summing up, it cannot be done. Yet, in all conscience it ought to be done. Therefore, the work must command adequate fees.

There is no other solution of the question than the education of the public, since most of us admit that the socialization of medical practice is a vague conception and far away from

us just now. The public must be trained to recognize that an "examination" or a diagnostic study is quite as concrete and valuable a service as a surgical operation, in many cases comparably difficult and expensive.

How can the public be educated?

First by that constant educational work that is being done by the individual practitioner, in personal contact with his patients. After all, the doctor is today more of a teacher than a medicine man, and of no type of practitioner is this more true than of the internist.

Secondly, writers from among our ranks should present the matter properly to the public through the common literary channels. The procedures and accomplishments of internal medicine, the importance and difficulty of modern diagnosis, should be discussed for the popular medical reader. The writer of this paper has been doing his best in that direction in the limited sphere in which his writings appear.

Thirdly, the organized efforts of internal medicine should be consciously directed at the problem. Every convention at which internists gather ought to organize one meeting of its period which is open to the public for the adequate presentation of these matters to laymen.

Beyond the application of the methods of modern efficiency to essential phases, the writer does not believe in any propaganda to build up the business side of our profession. But, as long as the work of the internist must be self-supporting, nothing but the efficient application of modern methods of thorough and complete diagnostic study to all cases that require it, is going to meet the ideal of an adequate service to the public on our part. Only a relatively small proportion of the cases that need this service, is getting it today. Internal medicine is not as yet properly organized to deliver it as surgery is being delivered. Yet, without modern diagnostic study of difficult and obscure conditions with a view to relief, and without the efficient recognition of early stages of serious diseases with a view to prevention, we are back in the dark ages of medical practice, and are failing to bring to the public the full benefit of modern scientific medical progress.

Editorial

ON THE "CAUSE" OF CANCER

There is no dictum of medical import more commonly in the mouth of the layman than that the 'cause' of cancer is unknown. Lawyers make unfair use of it in compensation cases and the presiding judicial officer falls readily into the same trap. The medical witness is asked if he knows the cause of cancer and he modestly replies in the negative. He is then asked if *anyone* knows the cause of cancer and the usual answer is that as far as he knows the cause of cancer is not known. The questioner then makes his point by asking if, since the cause of cancer is not known, it is not just as probable in the case in question that cancer was due to such and such a factor as to anything else; and the witness gives a feeble and unwilling assent, although his best judgment tells him that it was highly improbable that any causal relationship existed.

The difficulty lies in the form of the question itself. The cause of disease is always complex. It does not tell the whole truth to say that the cause of tuberculosis is the tubercle bacillus. Not only does the more immediate physical and humoral constitution of the host determine whether the disease is to develop, but the entire phylogenetic experience of the two interacting organisms lies back of that form of abnormal life and abnormal living that constitutes tuberculosis. Innumerable homely examples of the difficulty inherent in the form of the question can be found in everyday life. It is as though one had asked the cause of an elephant. In answer to such a query the keeper might think of the supply of provender which had been consumed during the long years of growth from birth to maturity; the geneticist of the union of the male and female reproductive cells with their intricate apparatus for the transmissal of unit characters, and the evolutionist of the millions of years of trial and error and success which have given to the elephant the huge bulk, thick skin, prehensile trunk and large ears which are part of his successful adjustment to his native habitat. But back of all this, and yet a part of it, as the chief cause of all, is life itself. It is equally true that life is a cause of cancer for the problems of neoplasia are the problems of *living* tumor cells descended from *living* body cells. Thus the question as to the cause of cancer is difficult, and in a sense impossible, to answer because its simplicity makes it profound.

Much is known, however, about factors which are concerned with the development of cancer and in one sense it may be said that the cause is known for the experimental pathologist can produce cancer at will. In suitable species of laboratory animals malignant neoplasms may be made to arise

de novo. The lines along which this success has been attained point the way toward a classification of the known carcinogenic factors in man. On the one hand carcinoma can be produced in suitable laboratory animals by selective breeding, and on the other by the application of various extrinsic agents, as exemplified by the historical induction of carcinoma of the stomach of the rat by Fibiger through feeding cockroaches containing a nematode worm (*Spiroptera neoplastica*), and of the ear of the rabbit by painting with tar (*Yamagiwa*), brilliant successes of the greatest significance which in more recent years have been paralleled by various other workers using several diverse procedures. Thus the known factors productive of neoplasms fall into two main groups, one containing those which are inherent or developmental, and therefore peculiar to the individual; and the other made up of the *extrinsic* agents. The first of these groups has in turn two aspects. It must be divided into those factors which are disturbances of development in the morphogical sense, *embryonal*, and those which are inherent in the genetic complexion of the individual, *intrinsic*. Thus it will be seen that the embryonal factors are developmental, the intrinsic factors are inheritable and the extrinsic factors are environmental.

The conception of an *embryonal* factor in the causation of neoplasms is of long standing (Cohnheim) and the list of tumors dependent in one way or another upon developmental defects such as the misplacement of simple or complex tissues, inclusion of tissue elements or even detached blastomeres (included twins), and the persistence of embryonic structures into post-fetal life, is constantly increasing. Many varieties of new growths, both benign and malignant, have their origin upon such a basis. The teratomas of testis and ovary, hypernephroma, adamantinoma, chordoma, the mixed salivary gland tumors and many others thus arise. Yet it is equally true that many of the most common forms of carcinoma such as those of the lip, gastro-intestinal tract and uterus cannot be thus explained.

The *intrinsic* factor stands in the forefront in the minds of many investigators today. Two great lines of evidence have supported it, the study of human inheritance as shown by certain so-called 'cancer families' (recently discussed in the ANNALS*), and the results of animal breeding experiments (Slye, Little, Lynch and others). The geneticists may differ among themselves as to the mendelian implication and interpretation of their results but there can be no doubt that under the conditions of the experimental laboratory the predisposition to the development of neoplasms can be bred in or out at the will of the trained investigator. Nor should it be expected that precise mendelian ratios will appear in such experimental series for the intrinsic factor is apparently a predisposing one only and the simultaneous operation of other factors must not be forgotten. There is some reason for believing that the intrinsic factor may be inherited in varying degrees of intensity.

*WARTHIN, A. S.: Heredity of carcinoma in man. Ann. Int. Med., 1931, iv, 681-696.

That many *extrinsic* factors are carcinogenic has long been recognized. Chimney sweeps' cancer of the scrotum, the kangri cancer of the shepherds of Thibet, the more recently recognized mule spinners' cancer and, within our own profession, the many examples of carcinoma of hands and face among the earlier roentgenologists have provided ample proof. These are but a few of the many occupational, accidental and experimental examples of the effect of such extrinsic agents. Mechanical, thermal, chemical and radio-active forces are all found in the list. Here, also, are examples of chronic infection providing the instigating factor, but only through such mechanisms as chronic irritation and exaggerated response to injury does infection cause cancer. There is almost complete agreement among investigators that there cannot be a specific extrinsic living organism, infection with which causes cancer. There are important theoretical objections to such an etiology that cannot be entered into here. It is significant that there is no proved example of the transfer of a neoplasm from patient to nurse, doctor, or to any member of the patient's family. But chronic inflammation due to infection, with excessive reparative proliferation such as may be associated with lupus, or at the mouth of a sinus or the border of an ulcer, may provide the extrinsic stimulus. It is from the field of occupational medicine that much of our knowledge of extrinsic carcinogenic factors has come. The list includes soot, tar, pitch, creosote, shale oil, petroleum, arsenic, aniline dyes, anthracene, radium, roentgen-rays, sunlight, burns of thermal, electrical and chemical origin, and repeated mechanical trauma.

The relative potency and the mode of interaction of the developmental, the intrinsic and the extrinsic factors we know relatively little about, although evidence of value in this respect is accumulating. For purposes of illustration and discussion a mathematical form is of use. If D represents the developmental (embryonic) factor, E the extrinsic factor and I the intrinsic factor, the following equations should be true:

(I) $I+D+E = \text{cancer}$,
(II) $I+E = \text{cancer}$,
(III) $I+D = \text{cancer}$.

Since both human family histories and animal breeding experiments include strains in which practically every individual succumbs to a malignant neoplasm it seems highly probable that, if the intrinsic predisposition is of a certain degree of intensity, or combined with a certain organ predisposition, either no extrinsic factor is needed or the ordinary minor environmental traumata may assume that rôle. The origin of cancer in such a case may be expressed by the equation

(IV) $I^n = \text{cancer}$.

It is not so clear whether or not cancer can ever develop in the absence of the intrinsic factor. That certain pioneer roentgenologists daily and many times a day, placed their hands before the fluoroscope to test the efficiency of their tubes and never developed cancer in spite of such protracted and intensive exposure may be due to the fact that they lacked the intrinsic predisposition.

If so, the equation

(V) $E^n = \text{no cancer}$

should be accepted as true. It might be a fruitful research to compare the family histories of the x-ray workers who developed cancer with the family histories of those who did not. If the intrinsic factor is necessary under such circumstances, may it not be true also, that

(VI) $D = \text{no cancer}$,
and (VII) $D + E = \text{no cancer}$?

Of this there is, as yet, no proof.

A brief survey of present opinion of the cause of cancer indicates that, after all, much has been accomplished and much is known. Members of the medical profession will do well to present such material to intelligent laymen and thus aid in dispelling the popular opinion that cancer research has reached an *impasse*. As Woglom put it not long ago, one need only ask a medical man whether he would rather have a carcinoma now, or thirty years ago, to learn whether there has been any progress in our knowledge of the cause, prevention, diagnosis and treatment of cancer during that period.

Abstracts

Blood Cultures and Focal Infections: An Experimental Study with One Hundred Healthy Adults. By Gordon C. Cameron, C. A. Rae and Geo. N. Murphy. (Canadian Med. Assoc. Jr., 1931, xxv, 131-134.)

Although it is generally assumed that the blood-stream of the healthy animal is normally free of bacteria there is much evidence, however, to indicate that pathogenic organisms do invade the blood-stream without necessarily producing disease. This is indicated by the frequent development of staphylococcic osteomyelitis following forms of trauma which could not effect the introduction of organisms. The subjects used in this investigation were presumably healthy young men who were interrogated as to present health and previous experience with disease. Inspection of the nose, throat and ears of each was carried out, as well as a detailed examination of the teeth with complete x-rays. A 20 cc. sample of blood from each subject was incubated with 180 cc. of beef heart infusion broth. These cultures were examined daily but were opened only after two weeks and four weeks of incubation. Of the 100 cultures, 81 remained without growth. Among the 19 showing growth it seemed certain that 12, and possibly 13, were contaminated. The remaining 6 showed growth of organisms believed to be derived from the blood. Four of these were characteristic of *Staphylococcus aureus* and the other two were "diphtheroids". Although there were 25 individuals in the group with x-ray evidence of apical disease of from one to four teeth, not one of the six positive cultures came from this group. One of the subjects who yielded a culture of *S. aureus* had a mucopurulent discharge from the right nostril, partial right nasal obstruction, a dim right antrum, enlarged tonsils and enlarged cervical nodes. The others were free of abnormalities which might be interpreted as disease except that two had a pustular acne on the back. While aware that the method used might fail to demonstrate certain of the more dependent parasitic organisms, it was chosen in order to permit speed and simplicity in manipulation.

Metastatic Tumors in the Thyroid Gland. By Rupert A. Willis. (The Am. Jr. of Path., 1931, vii, 187-208.)

In cases of systemic hematogenous dissemination of malignant tumors, the embolic influx into the various tissues must be proportional to their respective arterial blood supplies, yet such richly vascular organs as the intestine, spleen and thyroid gland are relatively infrequent sites for secondary growths resulting from hematogenous spread. Taking the total weights of the liver and thyroid to be 1500 and 25 grams respectively, it appears that the thyroid actually receives about one-half the volume of arterial blood received by the entire liver. Yet, while the liver is very frequently the seat of metastases derived from the systemic blood stream, metastatic growths in the thyroid gland are unusual. The author collected and reviewed the records of 47 examples of metastatic thyroid growths, and added 10 cases personally observed. He concluded that secondary tumors occur more frequently in the thyroid than they are generally recognized, partly due to failure to make thorough examination of this organ in doing autopsies upon the bodies of those dying of malignant disease. There are good grounds for believing that different tumor types possess different intrinsic capacities for establishing metastases in the thyroid and that melanomas and lung carcinomas are most potent in this respect. There is strong evidence that areas of abnormal thyroid tissue, such as adenomas, are predisposed to the establishment of metastatic neoplasms and that this predisposition depends on chemical or metabolic rather than on vascular changes in the altered tissues.

This predisposition on the part of pre-existing abnormal areas appears especially in connection with the metastases of neoplasms having relatively little tendency to colonize in the thyroid gland.

The Blood Sugar of Normal Fasting Persons. By B. Y. Glassberg. (Proc. Soc. Exp. Biol. and Med., 1931, xxviii, 889-893.)

The blood sugar values recorded generally in the literature represent the sum of the sugar and non-sugar reducing substances present. Somogyi has perfected a simple method of precipitation with zinc salts whereby, together with the blood proteins, the reducing non-sugars also are precipitated and thus filtrates are obtained that contain no appreciable amount of reducing substances other than sugar. Using such zinc filtrates, true sugar values are obtained in a single determination by any of the titrimetric or colorimetric methods in general use. The author determined the fasting true blood sugar in 100 normal adults, 50 men and 50 women. Samples were taken before breakfast, at least eight hours after the last meal. Somogyi's microtechnique for zinc precipitation combined with the Shaffer-Hartmann method was employed. Blood was obtained by puncture of the finger tip, the hand having been previously warmed in a basin of warm water. It was determined that capillary blood may properly be substituted for venous blood in determining the sugar of fasting individuals and that repeated squeezing of the finger to obtain successive samples did not modify the result through the admixture of other tissue fluids. The fasting true blood sugar of 50 men and 50 women was found to be between 70 and 95 mg. per 100 cc. of blood, with an average of 81.6 mg. The lowest blood sugar obtained was 70 mg., the highest 95.

Case of Pneumococcus (Type III) Meningitis Treated with Potassium Permanganate—Recovery. By Max H. Weinberg. (Jr. Nerv. and Mental Dis., 1931, lxxiv, 38-45.)

The very serious if not hopeless prognosis in pneumococcus meningitis has justified the use of various drastic methods of treatment such as continuous drainage, cisterna magna punctures, lavage of the ventricles and the injection of various irritating substances into the subarachnoid space. Stimulated by the results obtained by Chester in the treatment of pneumonia, as reported in the Annals in 1929, the author used potassium permanganate enemata in a case of meningitis shown bacteriologically to be due to pneumococcus, type III. A cleansing enema is first given followed by 4 ounces of the standard solution advocated by Nott, which contains 2 grains of potassium permanganate to one and one-half pints of water. Such enemata were given every four hours. The patient should lie on his left side and remain so for at least twenty minutes to facilitate retention. In the case described the patient made a rapid recovery and was practically normal eleven days after instituting treatment.

Suppression of Strychnine Convulsions by Barbiturates. By W. T. Dawson and Charles H. Taft, Jr. (Proc. Soc. Exp. Biol. and Med., 1931, xxviii, 917-918.)

Barbital (diethyl barbituric acid), phenobarbital (ethyl-phenyl), nembutal (ethyl-secondary amyl) and pernocton (B-bromallyl secondary butyl) were all found to possess the life-saving antagonistic action to strychnine poisoning which Zerfas and McCallum demonstrated for amytal (ethylisomyl barbituric acid). By starting the administration of these drugs with the onset of convulsions it was found possible to save the lives of rabbits which had received strychnine in an amount in excess of the certain lethal dose. Phenobarbital was much more effective than barbital when judged by the amount of the drug necessary to control convulsions.

Reviews

Sixty Centuries of Health and Physick: The Progress of Ideas from Primitive Magic to Modern Medicine. By S. G. Blaxland Stubbs and E. W. Bligh. With an Introduction by Sir Humphrey Rolleston. xvi + 253 pages, 64 plates. Paul B. Hoeber, Inc., New York City, 1931. Price, $5.00.

As Sir Humphrey Rolleston puts it in his introduction to this book, what embryology is to the study of man's structure and evolution, history is to the comprehension of an art or science. Thus it is easy to understand why the study of the History of Medicine has recently attracted more and more attention both in and outside the ranks of the medical profession. The present work, however, is by no means a history of Medicine in the usual sense. Rather it is an account of the growth and progress, the evolution of ideas, having to do with the search for health and its preservation. The preventive idea thus receives special emphasis throughout. While of necessity certain names and dates must appear, the pages are not made to bristle with them and the reader cannot lose sight of the progress of the central theme as the way is marked from primitive medicine to Metchnikoff, Banting and Theobald Adrian Palm, oftentimes by quotations from original sources. The illustrations are very well reproduced as full-page plates and add much to the value of the book. While written for the layman with an interest in the development of medical science, it should make an equally strong appeal to the medical man himself. Here is a book which the doctor can recommend to his lay friends as giving an interesting account of the development of modern preventive Medicine. We quote from the final paragraph: "It is often said that the future of Medicine is in the laboratory. Doubtless this is true, but it is through the agency of the devoted and observant practitioner that Health comes with healing in her wings. The problem will be to convey the knowledge gained in the laboratory to the one man who can put it to practical use."

The Doctor and His Investments: Financial Policy and Technique for the Physician. By Merryle Stanley Rukeyser, B. Lit., M.A., Financial Editor, Medical Economics and Dental Survey; Financial and Editorial Writer, New York American and Associated Newspapers; Associate in Journalism, Columbia University. ix + 330 pages. P. Blakiston's Son and Company, Philadelphia, 1931. Price $2.50 postpaid.

The doctor is faced with investment problems quite unlike those of the average business man. He cannot provide for the future by turning his profits back into his business. Even if he practices this by improving himself through graduate study and travel that investment dies with him; in fact, becomes useless when his active work ceases. The doctor must invest as a method of self-pensioning as well as for the purpose of providing for his family. Physicians as a class are readily susceptible to the suggestions of insincere advisers and doctors' names figure largely on the sucker lists of security charlatans. Well-meaning acquaintances and grateful patients find the doctor a childlike and trustful listener to amateurish financial advice, although he would be the last to select a medical consultant by that method. The book under review considers with sympathy and understanding the financial problems peculiar to the physician. The twenty-seven chapters are grouped in three parts dealing respectively with the Investment Policy for Doctors, Fields of Investment for Doctors and Fitting Investments to the Doctor's Needs. Throughout, a thorough knowledge of medical economics is revealed, particularly in such chapters as those which deal with equipping the doctor's office, with the pros and cons of Medical Arts Buildings and

with financial set-ups ensuring a proper perpetuation of clinical groups. A suitable life-term plan, an annual financial health examination, a proper diversification and a healthy conservatism are subjects receiving emphasis. Finally, definite financial prescriptions are offered for concrete cases covering the needs of the bachelor physician, the doctor with a family and the retiring medical man. This book deserves the fullest commendation. It can render a valuable service to all members of the profession.

Practical Dietetics for Adults and Children in Health and Disease. By SANFORD BLUM, A.B., M.S., M.D., Head of Department of Pediatrics and Director of the Research Laboratory, San Francisco Polyclinic and Post Graduate School. Fourth revised and enlarged edition. xi + 380 pages. F. A. Davis Company, Philadelphia, 1931. Price, $4.00 net.

This, the fourth edition of this work, differs from the preceding chiefly in the addition of a list of the chief sources of vitamines and a discussion of alkaline foods and diets. Detailed dietaries are given for healthy individuals of various types and conditions, as well as for those suffering from a variety of diseases. This book must prove of considerable use to the physician who is frequently called upon to give concrete advice, rather than broad suggestions, in dietary matters. The reader may grope, as does the reviewer, to learn why a spinster with impaired digestion is permitted to eat cauliflower but forbidden to eat cabbage (provided the mode of cooking is the same); or what difference in dietary value causes tongue muscle to be taboo for those who are encouraged to eat steaks, roast beef and roast mutton.

A Manual of the Common Contagious Diseases. By PHILIP MOEN STIMSON, A.B., M.D.; Associate in Pediatrics, Cornell University Medical College; Attending Physician, Willard Parker Hospital; Chief of Staff, the Floating Hospital of St. John's Guild; Chief of Clinic, Department of Pediatrics, Cornell Clinic, etc. xvi + 353 pages; 2 plates and 40 text figures. Lea and Febiger, Philadelphia, 1931. Price, limp binding, $3.75, net.

This manual was intended primarily as a clinical guide for medical students and internes but also includes the practical working directions needed by the nurse in charge of a patient with a contagious disease. It should be of great value to all practitioners and particularly to school physicians. Concisely written, it is also surprisingly complete. The diseases considered are diphtheria, Vincent's angina, scarlet fever, measles, rubella, whooping cough, mumps, chicken pox, vaccinia, epidemic meningitis and poliomyelitis. In addition there are chapters on the principles of contagion, serum reactions and the general management of contagious diseases. The size of the book is convenient and the binding durable and practical. This manual can be heartily recommended to those desiring a concise reference text on the common contagious diseases and their management.

Chronic Arthritis and Rheumatoid Affections with Recovery Record. By BERNARD LANGDON WYATT, M.D., F.A.C.P.; with the collaboration of LOUIS I. DUBLIN and foreword by DOCTOR J. VAN BREEMAN. ix + 166 pages. William Wood and Company, New York, 1930. Price, $2.50.

A chapter on the incidence of rheumatic disease is followed by one on types and causes, the two occupying 34 pages. Preventive measures and early diagnosis account for the next 22 pages. The remainder of this book deals with therapeutic procedures, particularly diet and physical agencies. Herein lies its value, for specific suggestions free from narrow prejudices are to be found. The author is fully alive to the futility of dietary fads, and the question of focal infection is treated with commendable restraint. At the end a number of blanks are provided upon which the patient may record progress notes, this procedure having been found to be of considerable value in securing his intelligent cooperation.

College News Notes

At the recent meeting of the American Society of Clinical Pathologists in Philadelphia, Dr. Walter M. Simpson (Fellow), Dayton, Ohio, was chosen as President-Elect of the Society.

Dr. Austin B. Jones (Fellow), Kansas City, Mo., was elected President of the Internist Club during the May meeting.

A Dermatologic Clinic on "Erythema Induratum", held by Dr. Ralph Bernstein (Fellow), Professor of Dermatology, Hahnemann Medical College of Philadelphia, was published in the July number of the Hahnemannian Monthly.

Dr. Harold L. Amoss (Fellow), Durham, N. C., has gone to Peiping, China, for a four months' stay, as Visiting Professor in the Peiping Union Medical College.

At the meeting of the 6th District Medical Society of the State of North Carolina, held in Durham on June 18, Dr. Robert L. Felts (Fellow), of Durham, was elected President for the ensuing year.

Dr. Thurman D. Kitchin (Fellow), Wake Forest, N. C., President of Wake Forest College and Dean of the Medical School of Wake Forest College, was recently appointed to serve on the Commission for the Improvement of the Laws of North Carolina, provided by the last General Assembly.

Dr. Verne S. Caviness (Fellow), Raleigh, N. C., read a paper on "The Early Diagnosis of Pellagra" before the North Carolina State Medical Society's meeting during April. This paper was published in the July Issue of Southern Medicine and Surgery.

Dr. Caviness also read a paper on "Blood Pressure" before the Johnson County (North Carolina) Medical Society on June 30.

Dr. Samuel W. Sappington (Fellow), Philadelphia, is the author of an article, "Death's Time Table and Passing Remarks," which was published in the July issue of the Hahnemannian Monthly.

Dr. Clement C. Fihe (Fellow), Cincinnati, Ohio, was one of the guest speakers at a recent meeting of the Bourbon County (Ky.) Medical Society.

The North Carolina Radiological Society was recently formed with the following Fellows of the College holding offices:

Dr. J. K. Pepper, Winston-Salem—President

Dr. W. T. Rainey, Fayetteville—Vice-President

Dr. Sylvester D. Craig (Fellow), Winston-Salem, N. C., was elected a member of the State Board of Health during the recent meeting of the North Carolina State Medical Society.

Dr. Thomas E. Rogers (Fellow), Macon, Ga., read a paper on "Diagnosis and Treatment of Cardiac Arrythmias" before the Sixth District Medical Society, which met on June 24 at Indian Springs.

Dr. LaRue D. Carter (Fellow), Indianapolis, addressed the Jay County (Indiana) Medical Society, July 2, on "Muscular Dystrophy."

Dr. Thomas W. Oberlin (Fellow), Hammond, was elected President of the Indiana State Board of Health for two years, during a reorganization meeting on July 2.

Dr. Henry G. Rudner (Fellow), Memphis, Tenn., on June 18 addressed the East Mississippi Medical Society, Philadelphia, on "Symptoms of Colon Infection."

Main entrance to Duke Hospital of the Duke University School of Medicine, showing the Seal of the American College of Physicians above the door at the right and the Seal of the American College of Surgeons above the door at the left.

DEDICATION OF THE

DUKE UNIVERSITY SCHOOL OF MEDICINE

AND THE

DUKE HOSPITAL

ON

April 20, 1931.

The new Duke University School of Medicine and the Duke Hospital were fittingly dedicated at Durham, N. C., with an elaborate program. The erection of the School of Medicine and the Hospital marks another completed step in a far-reaching program conceived by Washington Duke and further advanced by his sons, Benjamin N. and James B. Duke, the latter of whom is directly responsible for the munificent gift founding the Duke University School of Medicine and the Duke Hospital in 1925. The cost of erecting the buildings for the School of Medicine and Hospital exceed four million dollars, leaving an endowment of six million dollars for maintenance. The architecture of all buildings is Gothic; there is but one architect for all the University buildings, resulting in a symmetry of design seldom carried out so fully in other American universities.

The wards in the new Duke Hospital have been named for distinguished physicians and surgeons, largely of the South, as follows: William H. Welch, the only living physician for whom a ward is named, and who attended the dedication exercises; Sir William Osler, noted physician who made his home in Maryland for many years; Josiah Clark Nott, of South Carolina; Daniel Drake, of Kentucky; Walter Reed, of Virginia; William Stewart Halsted, of Maryland; Edmund Charles Fox Strudwick, of North Carolina; Crawford Williamson Long, of Georgia; Ephraim McDowell, of Kentucky; James L. Cabell, of Virginia; J. Marion Sims, of South Carolina; Francois Prevost, of Louisiana, and Henry Fraser Campbell, of Georgia.

Dr. Wilburt C. Davison (Fellow) is Dean of the Duke University School of Medicine. Other Fellows connected with the School are Dr. Harold L. Amoss, Professor of Medicine; Dr. William DeB. MacNider, Chapel Hill, N. C., Visiting Lecturer in Special Pharmacology; Dr. P. P. McCain, Sanatorium, N. C., Visiting Lecturer in Medicine.

Dr. John E. Greiwe (Fellow), Cincinnati, gave an illustrated lecture on "The Influence of the Peripheral Circulation" before the Darke County (Ohio) Medical Society on May 8.

The 84th semi-annual joint meeting of the Miami and Shelby County (Ohio) Medical Societies was addressed on June 4 by Dr. Walter M. Simpson (Fellow), Dayton, on "Recent Developments in Undulant Fever."

Dr. Byrl R. Kirklin (Fellow), Rochester, Minn., was a guest speaker during the meeting of the Norfolk County (Va.) Medical Society on June 1; the subject of his paper was "Gastric and Duodenal Ulcers."

Dr. Jay A. Myers (Fellow), Minneapolis, addressed the Washington Tuberculosis Association at Wenatchee, June 11-13, on tuberculosis problems.

Dr. John T. Strawn (Fellow), Des Moines, Ia., spoke on "Gastric and Duodenal Ulcers" before the Madison County (Ia., Medical Society on June 8.

Beginning August 17, Dr. Carl J. Wiggers (Fellow), Cleveland, Ohio, conducted a vacation course on the principles and practice of electrocardiography at Western Reserve University School of Medicine.

Dr. Henry H. Turner (Associate), Oklahoma City, was among the speakers at the meeting of the Southeastern Oklahoma Medical Association on June 24. The title of his paper was "Ether Anesthesia."

Dr. James S. McLester (Fellow), Birmingham, Ala., addressed the Chattanooga and Hamilton County (Tenn.) Medical Society, July 9, on "Protein Quota in Health and Disease."

Dr. Ray C. Blankinship (Fellow), Madison, Wis., spoke on "Colitis" before the Mar-

inette-Florence County (Wis.) Medical Society on July 9.

Dr. George B. Eusterman (Fellow), Rochester, Minn., will address the ninetieth annual meeting of the State Medical Society of Wisconsin, September 9-11, on "Carcinomatous Gastric Lesions Masquerading as Benign Ulcer."

A portrait, the work of Thomas C. Corner, of Baltimore, of Major General Merritte W. Ireland (Fellow) was unveiled in connection with a farewell reception given Dr. and Mrs. Ireland, May 29, at the Army Medical Center, on the occasion of his retirement as Surgeon General of the U. S. Army. The portrait will hang in the Administrative Offices of the new building of the Army Medical School.

Col. Matthew A. Delaney (Fellow), Fifth Corps Area, Fort Hayes, Columbus, Ohio, beginning January 1, 1932, will be Assistant to Surgeon General Robert U. Patterson of the U. S. Army, and will be advanced to the rank of Brigadier General. Col. Delaney was formerly Assistant Executive in the Surgeon General's Office. During the World War, he served, first, in charge of Base Hospital No. 10, and later as Liaison Officer with the British War Office. He was the recipient of the Distinguished Service Medal, and also was decorated by the British Government.

Col. Charles F. Craig (Fellow), after a service of thirty-three years, at his own request, has been retired from the Medical Corps of the U. S. Army. He has accepted the appointment as Professor of Tropical Medicine and Director of the Department of Tropical Medicine at Tulane University of Louisiana School of Medicine.

Col. Craig is a graduate of Yale University School of Medicine. He did postgraduate work in the Bureau of Science, Manila, and in the Rockefeller Institute for Medical Research. From 1910-1911, he was Assistant Professor of Bacteriology at Yale University School of Medicine; from 1909-1922, Associate Professor and Professor of Bacteriology, the Army Medical School; from 1920 to recently, he was Professor and Director of the Department of Laboratories and Preventive Medicine at the Army Medical School. During the World War, he received the Distinguished Service Medal.

In addition, Col. Craig served four years as Commanding Officer of the Central Department Laboratory, Fort Leavenworth, Kansas, one year in charge of the Departmental Laboratory at El Paso, Texas, and four years as Medical Inspector in Hawaii.

TULANE ESTABLISHES NEW DEPARTMENT OF PREVENTIVE MEDICINE

Announcement has recently been made that Tulane University of Louisiana School of Medicine has established a new Department of Preventive Medicine in connection with "the Commonwealth Fund of New York through which the University will participate in the rural health program recently initiated in Mississippi by the fund. An annual appropriation of $25,000 has been allotted by the fund to the School of Medicine to establish the new department and to encourage attention to preventive medicine in other clinical departments. Five free scholarships have been established for undergraduate medical students from Mississippi, providing the student with $1,200 a year for four years, with the requirement that after graduation he shall practice at least three years in Mississippi. In addition, fifteen practicing physicians will be sent each year to Tulane for four months' graduate work. Their tuition and transportation to and from New Orleans will be paid by the fund, and they will be allowed a monthly stipend of $250." The arrangement with Tulane is said to be similar to that made with Harvard University Medical School for practitioners of Massachusetts.

Acknowledgment is made of the following gifts of reprints and books by members to the College Library:

Dr. Oscar W. Bethea (Fellow), New Orleans, La.—4 reprints.

Dr. Orville H. Brown (Fellow), Phoenix, Ariz.—11 reprints.

Dr. John L. Chester (Fellow), Detroit, Mich.—1 book, "Rheumatic Fever—A Heart Disease."

Dr. Edward E. Cornwall (Fellow), Brooklyn, N. Y.—1 reprint.

Dr. Oswald E. Denney (Fellow), Carville, La.—12 reprints.

Dr. J. L. Goforth (Fellow), Dallas, Texas—10 reprints.

Dr. George R. Herrmann (Fellow), Galveston, Texas—1 bound volume containing sixty-two reprints.

Dr. Thomas Hall Shastid (Fellow), Duluth, Minn.—1 reprint.

Dr. William H. Strietmann (Fellow), Oakland, Calif.—1 reprint.

OBITUARIES

DOCTOR LEONARD NAPOLEON BOSTON

Dr. Leonard Napoleon Boston (Fellow), a widely known physician of Philadelphia, died on July 4, 1931, at the age of fifty-nine years. Born in Shickshinny, Pennsylvania, on March 18, 1872, the son of Alfred H. and Bethiah (Bacon) Boston, a daughter of Rev. Septimus Bacon, who served in the War of 1812, Dr. Boston was educated at Huntington Mills Academy, Minneapolis High School and Atchison Commercial College, Atchison, Kansas. He taught school and attended college conjointly prior to entering the Medico-Chirurgical College, from which he was graduated in 1896. In 1895 Dr. Boston was graduated from the Philadelphia School of Anatomy with highest honors; in 1902 he received the honorary degree of A.M. from Ursinus College.

Two years after taking his medical degree, Dr. Boston became the Bacteriologist to the Philadelphia General Hospital, a position he held for six years. In 1901 he was appointed Bacteriologist of the Ayer Clinical Laboratory, Pennsylvania Hospital. He was Director of Clinical Laboratories at the Medico-Chirurgical College from 1901 to 1905. In 1906 Dr. Boston was appointed Director of the Clinical Laboratories of Research of the American Hospital for Diseases of the Stomach and soon thereafter became Pathologist at the Frankford Hospital. One year previously (1905) he was married to Miss Caroline Crandall of Westerly, Rhode Island.

Whilst Dr. Boston quite early directed his attention to bacteriology and later pathology, he at no time forsook the clinical aspects of medicine for the laboratory side. For example, from 1897 to 1899 he was Instructor in Obstetrics at the Medico-Chirurgical College, Instructor of Medicine in the same school from 1899 to 1901; Associate in Medicine in 1904 and Adjunct Professor of Medicine from 1905 until 1912 when he was elected to a newly created chair of Physical Diagnosis; this professorship he continued to hold in the Medico-Chirurgical College, Graduate School of Medicine of the University of Pennsylvania, until 1817 when he became Assistant Professor of Medicine in the latter school, holding that position until his untimely death.

At the time of his demise, Dr. Boston was Professor of Principles and Practice of Medicine and Clinical Medicine in the Woman's Medical College of Pennsylvania; this important chair he had worthily filled since 1928. For a quarter of a century he was one of the physicians to the Philadelphia General Hospital. Here he gave much of his time and energy to bedside teaching—a form of instruction in which he excelled.

Dr. Boston was an author of note. In 1904 he published a text-book on "Clinical Diagnosis by Laboratory Methods." He was co-author with the writer of a text-book of "Medical Diagnosis," which appeared in 1911, and passed through three editions. He built up his enviable and well-earned reputation as practitioner, consultant, author and teacher, by his tireless energy and native ability, as well as high ethical ideals. Doubtless, he owed

some of his success to his unfailing courage and optimism.

Toward his patients, he ever manifested deep human sympathy and at all times he radiated moral qualities which endeared him to his numerous friends. At social and professional gatherings, Dr. Boston was a retiring figure, although upon being engaged in conversation was both entertaining and interesting, revealing an unusual fund of general and scientific knowledge. It is to be recollected, however, that his higher qualities of excellence emanated from the heart.

Dr. Boston was the author not only of text-books, but of upwards of sixty scientific papers, many of which showed his bent for original laboratory and clinical observations. He held membership in many scientific societies and clubs, among which were the College of Physicians of Philadelphia, the Philadelphia County Medical Society, Medical Society of the State of Pennsylvania, the American Medical Association, American College of Physicians, Pathological Society of Philadelphia, the Society for the Study of Allergy, the Society of the War of 1812, the Sons of the American Revolution, the University Club and the Rotary Club of Philadelphia.

After he was graduated in medicine, Dr. Boston settled in Philadelphia and took up general medicine. At the same time he became the office assistant to the writer for a period of seven years. During that period he manifested remarkable industry and loyalty, performing every duty with absolute fidelity. His subsequent career was characterized by assiduous activity and devotion to the many duties devolving upon him, until interrupted by the appearance of a serious cardio-vascular condition which, during the last four months of his life, incapacitated him from professorial and other professional duties. During this closing period of his busy life, coronary occlusion, most probably due to an atheromatous condition of the root of the aorta and the coronaries, developed.

Surviving him are Mrs. Caroline Crandall Boston, his widow, a daughter, Miss Barbara C. Boston, a sister, Mrs. Myrtle B. Eyler, and a brother, Dr. C. A. Boston.

(Furnished by J. M. Anders, M. D., M.A.C.P.)

DOCTOR JAMES P. SCHUREMAN

Dr. James P. Schureman (Fellow), New Brunswick, N. J., died, May 6, 1931; aged, 51 years.

Dr. Schureman graduated from Princeton University in 1901, and from the University of Michigan Medical School in 1905. He was one of the most prominent physicians in Middlesex County, and was the first Fellow of the American College of Physicians in this part of New Jersey. He was highly respected by his colleagues and by the citizens of New Brunswick.

Dr. Schureman was a man of charming personality, unselfish, most conscientious and devoted to the interests of his family and friends as well as patients. His family has been prominent in New Brunswick for nearly two hundred years. Dr. Schureman was an Attending Physician on the Staffs of St. Peter's General Hospital, Middlesex General Hospital and

Parker Home. He was a Fellow of the American Medical Association, a member of the New Jersey State Medical Association and of the local societies. He had been a Fellow of the American College of Physicians since 1925.

Although interested in civic affairs and a Trustee of the Anable School, Dr. Schureman devoted practically his entire time to his professional work (Internal Medicine) and hospital affiliations.

(Furnished by Frederick L. Brown, M.D., F.A.C.P., New Brunswick, N. J.)

Variations in Manifestations of Rheumatic Fever in Relation to Climate*

By Warfield T. Longcope, M.D., F.A.C.P., *Baltimore, Md.*

THE statement can frequently be found in textbooks and monographs that rheumatic fever is ubiquitous. This generalization (which is often attributed to Hirsch[1]) can, however, scarcely be accepted today. Aside from the interest which has always been aroused by the seasonal incidence and familial occurrence of rheumatic fever, as well as the yearly variations in the severity of the disease, there has recently been some attempt to study, more accurately than has been possible before, the geographical distribution of the disease. The matter is one of importance not only in relation to rheumatic fever but in connection with other diseases. It is now well recognized, for instance, that infections such as scarlet fever and diphtheria, so common in the temperate zones, are almost unknown in some tropical countries. The geographical distribution of pernicious anemia, also, is very irregular. It is said to be almost unknown in China and Japan (Mills[2]).

My interest in possible climatological differences in the symptomatology of rheumatic fever was awakened, almost ten years ago, on coming to Baltimore from New York. Arthritis was often the predominant symptom of acute rheumatic fever in the adult in New York, and the one for which the patient called the physician or entered the hospital. Combined with the severe arthritis, or sometimes without severe arthritis, there was not infrequently observed acute, severe, and sometimes fatal endocarditis, pericarditis, myocarditis, pleurisy and pneumonia.

In Baltimore, on the other hand, the acute severe arthritis, so familiar in New York, was rarely encountered in the wards of the hospital. In general, though the disease seemed common in Baltimore, it presented a somewhat different clinical picture, appearing more insidious, less outspoken in its arthritic manifestations, not so fulminant in its severer forms, but suggesting usually a chronic or relapsing progressive disease of the heart. In order to obtain more definite information on these points, the case histories of patients with rheumatic fever treated during the last five years in the adult medical wards of the Johns Hopkins Hospital have been analysed.

*From the Medical Clinic, the School of Medicine, Johns Hopkins University and Hospital. Read at the Baltimore Meeting of the American College of Physicians, March 23, 1931.

It is difficult, as Newsholme[3], who was interested in this question, found many years ago, to obtain accurate information regarding the regional distribution of rheumatic fever throughout the world. The statistics collected from hospitals by Faulkner and White,[4] by Harrison and Levine,[5] and by Seegal and Seegal[6] indicate that rheumatic fever is commoner and more severe in the colder portions of the temperate zones than in the warmer portions. Seegal and Seegal also found that the incidence of rheumatic fever was greater from 1916 to 1918 than from 1918 to 1925. Excellent as these statistics are, they are based on diagnoses made in a variety of hospitals, and one cannot help but wonder upon what criteria the diagnoses were made. Do these statistics represent only those cases of rheumatic fever presenting arthritis, or do they include all cases of rheumatic fever? It is usually assumed that practically all cases of mitral stenosis are instances of rheumatic fever in the active, quiescent or healed stage of the disease. It is therefore very important in investigating the geographical distribution of rheumatic fever to know the regional distribution of mitral stenosis. Meleney and Kellers[7] state that though rheumatic arthritis is rare in China, mitral stenosis is common. Harrison and Levine found mitral stenosis frequent in Boston, St. Louis and Baltimore, much less frequent in Galveston, Richmond and Oklahoma, and rare in New Orleans. Wood, Jones and Kimbrough[8] find rheumatic fever and rheumatic heart disease about half as common in Virginia as in Massachusetts. Clarke[9] believes that rheumatic fever is almost unknown in natives in the tropics, defining the tropics as an area lying between 23° 28′ North and South. He states that he did not see a single case of rheumatic heart disease among 150,000 hospital cases in Perak, Malay States. Coburn[10] quotes Getz as stating that in the last 4 years only three unquestioned cases of rheumatic pancarditis have been recognized at autopsy at the Hospital of Santo Tomas in Panama. According to Coburn, rheumatic fever is extremely rare in Porto Rico. In about 500 autopsies studied by Dr. Lambert and Dr. Pappenheimer no gross or microscopic lesions of rheumatic fever were found. In a later series, however, two autopsies showing rheumatic pancarditis have been recorded.

The information, therefore, that is obtainable through published statistics and from such important personal surveys as that made by Coburn, goes to show that rheumatic fever, in all its forms, is exceedingly rare in the tropics, though rheumatic heart disease is not unknown in some tropical countries; whereas all the manifestations of rheumatic fever are common in the colder portions of the North and South temperate zones, where rheumatic arthritis is particularly prominent. In the intermediate and warmer regions of the temperate zones, rheumatic fever is certainly not recognized with as great frequency as it is in the colder regions. The geographical distribution, according to Coburn, corresponds to that of scarlet fever.

In analysing the cases at the Johns Hopkins Hospital, rheumatic fever ha-

been considered as a generalized disease, and consequently there have been included in this category all instances of chorea, of mitral stenosis, of rheumatic pancarditis and of rheumatic arthritis, whether they have been observed in the active, quiescent or possibly healed stages of the disease. In the majority of the cases there was some definite evidence of activity while the patient was under observation in the hospital wards. It may be seen from Table I that rheumatic fever is quite common in Baltimore, for 1.37 per cent of all patients admitted to the adult medical wards suffer from rheumatic fever. The cases of rheumatic fever, moreover, form a fair proportion of all autopsies, at least 1.66 per cent. The figures for the admission rate are a little higher than those given by Faulkner and White for the Peter Bent Brigham Hospital in Boston (Table II).

TABLE I
ADMISSION OF RHEUMATIC FEVER TO ADULT MEDICAL WARDS

Five Year Period—Sept. 1st, 1925 to Oct. 1st, 1930.

Total Admissions =	10,385
Rheumatic Fever =	142
Admission Rate =	1.37%
Total Autopsies 1908-1929 =	8,164
Total Rheumatic Carditis =	146
Per Cent Rheumatic Carditis =	1.6

Since 36 of the 146 autopsies showed rheumatic heart disease in acute or subacute form, it may be inferred that the disease may occur in Baltimore as an acute and severe infection. The total mortality for the 142 cases was 16.2 per cent. Table III shows the age incidence at the

TABLE II
REGIONAL DISTRIBUTION OF RHEUMATIC FEVER
(Modified from Faulkner and White)

PLACE	Av. Yearly Med. Admis.	Rheumat. F. Chorea	Per Cent
Johannesburg, S. Africa	2,906	169	5.8
Glasgow Royal Infirmary	2,655	126	4.74
Mt. Sinai, N. Y.	1,641	58	3.6
Royal Prince H., Australia	1,966	58	2.9
London Hospital	10,273	274	2.7
Univ. Hosp., Iowa	1,537	38	2.4
P.B.B. Hosp., Boston	2,486	31	1.3
J. H. Hosp., Baltimore	1,723	23	1.37
Univ. Hosp., Omaha	760	5	0.7
Barnes Hosp., St. Louis	1,358	6	0.47
Charity Hosp., New Orleans	5,349	28	0.4
Univ. Hosp., Atlanta, Ga.	2,500	2	0.08

TABLE III
142 CASES OF RHEUMATIC FEVER

Age	Total Cases	Auricular Fibrillation	Heart Block	Bacterial Endocarditis	Deaths
0-20	49	3	9	3	13
21-30	40	4	3	6	7
31-40	33	12	6	2	8
41-50	14	11	1		3
51+	6	6		1	2
Total	142	35	19	12	23
Per Cent		25.3	13.4	8.5	16.2

Parker Home. He was a Fellow of the American Medical Association, a member of the New Jersey State Medical Association and of the local societies. He had been a Fellow of the American College of Physicians since 1925.

Although interested in civic affairs and a Trustee of the Anable School, Dr. Schureman devoted practically his entire time to his professional work (Internal Medicine) and hospital affiliations.

(Furnished by Frederick L. Brown, M.D., F.A.C.P., New Brunswick, N. J.)